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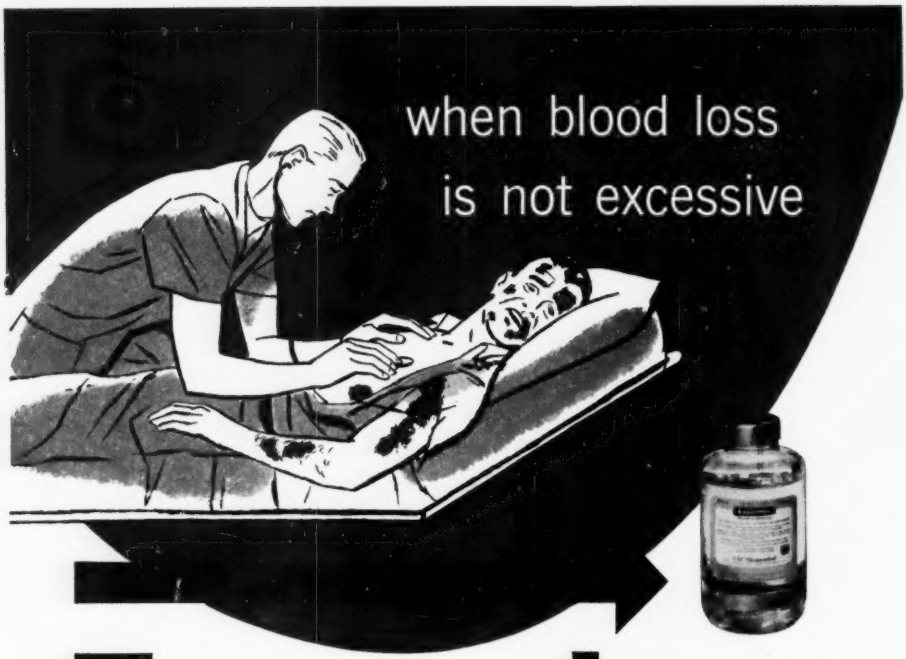

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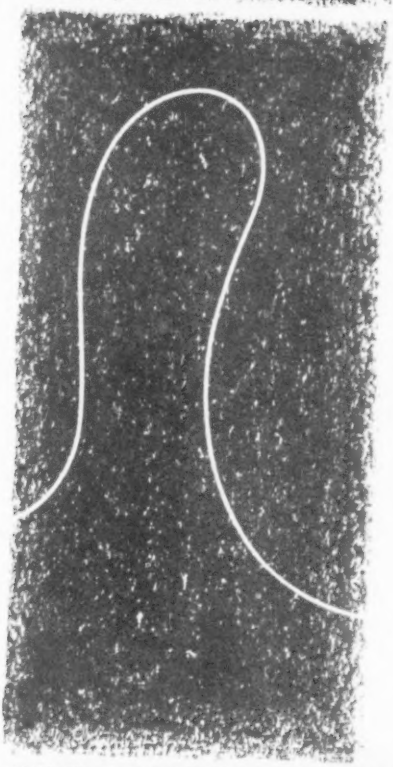

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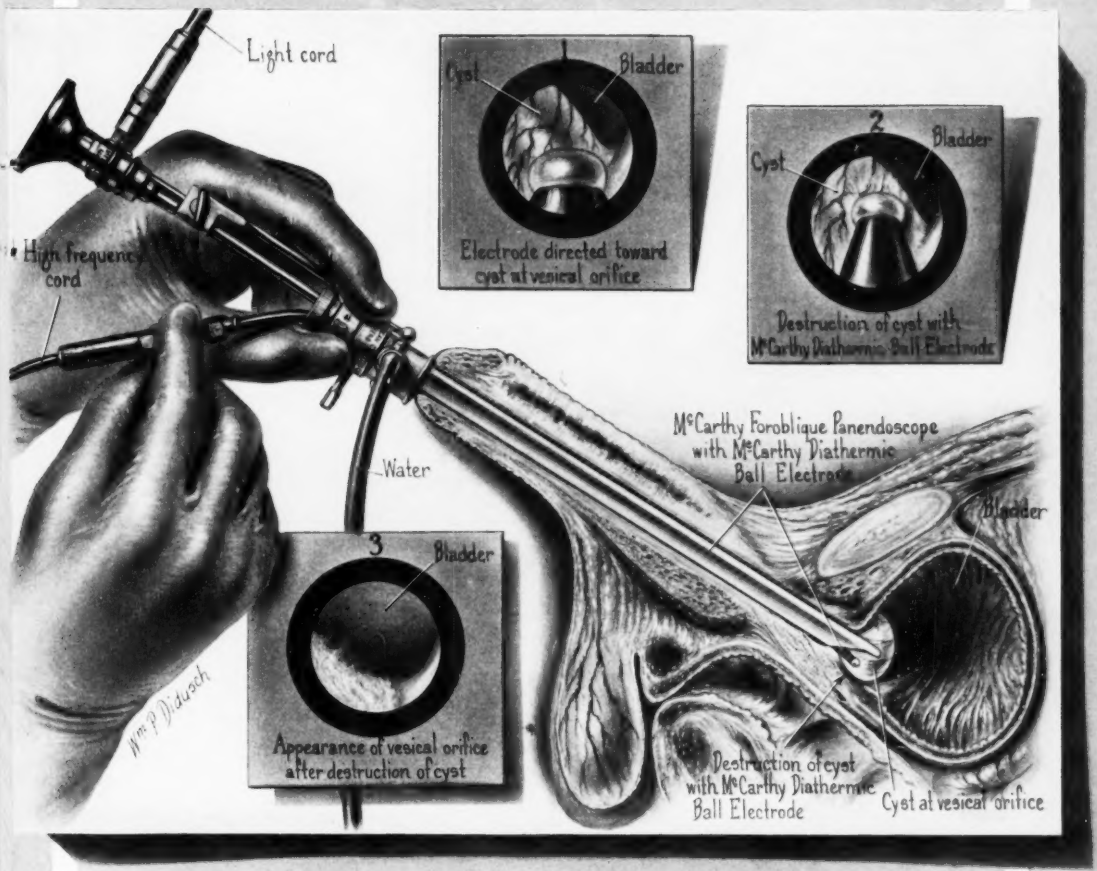

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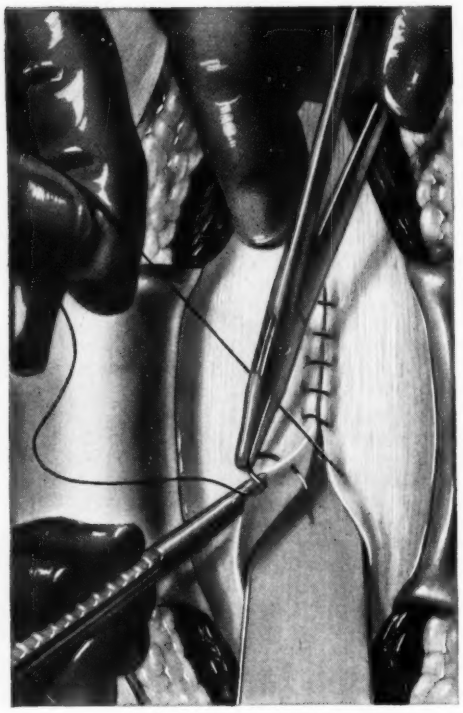

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Editorials

A VARIATION IN THE TECHNIQUE OF SUBTOTAL GASTRIC RESECTION FOR PEPTIC ULCER

THE MASS of both clinical and experimental data dealing with the ulcer problem has become so vast that an occasional brief historical review is indicated if present procedures are to be evaluated properly.

In spite of an almost continuous introduction of new drugs, most internists will agree that patients with ulcers today may be temporarily healed, some permanently controlled, but none permanently cured by medical means. Indeed, many internists are becoming more surgically minded as to the problem of peptic ulcer.

That subtotal gastric resection continues to find a place in the treatment of peptic ulceration is evidenced by the large number of articles in the current surgical journals dealing with this method of treatment.

Whereas many factors undoubtedly play a part in the genesis of ulcer, it is now generally agreed that hypersecretion of acid-pepsin digestive juices is one of the essential factors. Both the medical and surgical treatment of ulcer aim to reduce the amount of acid-pepsin secretion.

In the days when simple gastroenterostomy was the procedure of choice, neutralization of the gastric contents was considered to be all that was required. The subsequent frequent occurrences of jejunal ulceration showed this method to be inadequate, and subtotal gastric resection became the vogue. Early resections included only the pyloric end of the stomach and were based on Edkin's discovery of the hormone gastrin secreted by this portion of the stomach, which in turn stimulated the secretion of the acid-pepsin cells of the body of the stomach. The existence of this hormone, though disputed by some, has recently been confirmed by Dragstedt.

The clinical experience of many surgeons soon showed that removal of only the pyloric end of the stomach did not sufficiently reduce the acid-pepsin secretion to prevent the recurrence of jejunal ulceration in all cases. This led surgeons to increase the extent of the resection to include larger and larger portions of the acid-secreting area of the stomach, which reached its end point in Wangensteen's close to total gastrectomy. This solved the problem of preventing recurrent ulceration but added in numbers to the complication known inelegantly as the "dumping syndrome," which in extreme cases caused the sufferer more anguish than his original disease.

The remaining problems then are to reduce acid-pepsin secretion to the proper point and to prevent dumping by retaining the reservoir function of the remaining gastric pouch.

From the Department of Surgery, Stanford University School of Medicine.

In 1929 Connell introduced a new concept in the principle of surgical treatment of ulcer. Accepting the importance of the acid-pepsin factor in the production of ulcer, he recommended removing a large portion of the acid-secreting area and at the same time retaining the alkaline-secreting antrum and the pyloric sphincter. He did this by making a wedge-shaped excision of the body of the stomach with the apex of the wedge close to the lesser curvature but not dividing it.

More recently, Wangensteen has adopted Connell's concept of the desirability of removing the acid-secreting area of the stomach and leaving the gastrin-secreting area. He accomplishes this by extending the old segmental resection of Mikulicz to include the entire body of the stomach, leaving the pyloric antrum and a small portion of the fundus, which are then united in continuity. To overcome the effects of the resulting interference in motility, he widens the pylorus by means of an extensive Heineke-Mikulicz procedure.

Connell's and Wangensteen's operations have not been accepted by the surgical profession even though their results have been good. The time has been short and the number of cases too small for other surgeons to adopt these procedures in view of the fact that orthodox subtotal gastric resection, while admittedly not perfect, has stood the test of time and will not be superseded until another procedure has been proved superior by the same demanding tests.

Cox and other investigators showed that the acid-secreting cells of the stomach are concentrated in the body of the organ and along the greater curvature well into the pyloric zones, and that they are fewer in number in the fundus and along the lesser curvature. Because of the large mucosal folds in the body of the stomach and along the greater curvature, excision of this part of the stomach will remove considerably more acid-secreting area than a measurement of the corresponding serosal surface would indicate.

Largely on the basis of Cox's work, we began about two years ago to resect a larger portion of the greater curvature, while retaining more of the lesser curvature—the direct opposite of the Hofmeister-Finsterer resection, in which the lesser curvature is excised. To describe the operation briefly, the lesser curvature is freed to just above the angle of the stomach and a clamp is placed at right angles to the lesser curvature to include a sufficient amount of the stomach for satisfactory anastomosis. A second clamp is then applied at an angle along the greater curvature so as to remove the desired amount of this part of the stomach. The portion of stomach included in this clamp is then closed and the anastomosis made to the stomach adjacent to the lesser curvature as a Billroth-II procedure.

Shortly after beginning to do this operation, we found that in 1940 Zollinger [1] had done the same operation and for the same basic reasons. He performed this operation with good results in two patients with jejunal ulcers.[2]

To date the results in our series of this operation have been very satisfactory, though the small number of cases, a total of 53, and the short time involved, all within less than two years, are not sufficient to permit any final conclusions. All

1. Zollinger, R.: Gastric Resection with Removal of the Fundus in the Treatment of Duodenal Ulcer, Surgery **8**:79-93, 1940.

2. Further references to this operation will be found in Nagel, G. W.: Subtotal Gastric Resection for Peptic Ulcer, California Med. **78**:189-193, 1953.

cases showed a relatively high preoperative acidity and above normal uropepsin determinations, which postoperatively were reduced to below normal. No case of the "dumping syndrome" has occurred, and both clinically and roentgenologically, a satisfactory reservoir function of the stomach has been retained.

As our present comments deal with subtotal gastric resection, a flash comment only will be made on vagotomy as a method of reducing gastric secretion. In the main, adequate protection against recurrent ulceration is obtained without additional vagotomy. In two instances where previous gastric surgery had failed, a vagotomy was added to the procedure. In 50 cases a short-loop retrocolic Billroth-II type of anastomosis was done. In three cases a Billroth-I anastomosis was made.

The method of subtotal gastric resection for peptic ulcer which removes a large part of the greater curvature of the stomach and retains much of the lesser curvature, while representing a minor technical change from the commonly used methods of resection, appears to be based on sound anatomical and physiological practices.

GUNTHER W. NAGEL, M.D.

SURGICAL TREATMENT OF ARTERIOSCLEROTIC ANEURYSMS OF THE ABDOMINAL AORTA

JOHN W. KIRKLIN, M.D.
JOHN M. WAUGH, M.D.
JOHN H. GRINDLAY, M.D.
CALVIN R. OPENSHAW, M.D.
AND
EDGAR V. ALLEN, M.D.
ROCHESTER, MINN.

ARTERIOSCLEROTIC aneurysms of the abdominal aorta present as serious a challenge to surgeons today as they have at any preceding time, although the reasons for this situation are different from those pertaining as recently as 15 years ago. Whereas in the past the details of operative technique successfully challenged the surgeon, the current methods of surgical treatment of vascular diseases are sufficiently refined to permit direct as well as indirect attacks on such aneurysms. Pressing problems remain that are no less urgently in need of settlement than are the purely technical ones. These have to do with indications for operation in abdominal aortic aneurysm, selection of the type of procedure to be used, and evaluation of the efficacy of the operative procedures under consideration in the alleviation of symptoms and the prolongation of life.

This paper presents experience with the operative treatment used in 23 patients who had aneurysms of the abdominal aorta; these patients represent all those operated on by us at the Mayo Clinic up to May 15, 1953. During the time covered by this study, no patients who had such aneurysms were denied the opportunity of operation, although one patient who had an acutely leaking aneurysm refused operation and died 10 days later. Three different types of operations were performed. The data in these cases will be discussed and compared with the experiences of other surgeons in an attempt to aid solution of the problems just highlighted.

OPERATIVE TECHNIQUES

The 23 patients were cared for by two different surgical services. It had been decided that one surgeon (Waugh) would give a thorough trial to reinforcement of the aneurysms with nonabsorbable polyvinyl sponges (Ivalon), as described

Read before the Section on Surgery, General and Abdominal, at the 102nd Annual Session of the American Medical Association, New York, June 2, 1953.

From the Division of Surgery (Drs. Kirklin and Waugh), the Section of Surgical Research (Dr. Grindlay), and the Division of Medicine (Dr. Allen), Mayo Clinic, and Fellow in Surgery, Mayo Foundation (Dr. Openshaw).

by Grindlay and Waugh.[1] The other surgeon (Kirklin) would attack the aneurysms, when feasible, by thromboendarterectomy and wrapping; more recently, resection and grafting were used. Although the entire series is used in compiling rates for operative mortality, only those patients operated on prior to Jan. 1, 1953, are included in the follow-up studies.

Thromboendarterectomy.—The method for thromboendarterectomy and wrapping used by us is that described by Wylie and his associates.[2] The operation was done through a long midline abdominal incision, which passed to one side of the umbilicus. Exposure was obtained by elevation of the transverse mesocolon and packing the small bowel and cecum to the right and the sigmoid and descending colon to the left (Fig. 1). The transverse portion of the retroperitoneal part of

Fig. 1.—*a*, Exposure for operation on arteriosclerotic aneurysm of abdominal aorta. *b*, Schematic cross section through aneurysm.

the duodenum was mobilized away from the anterior surface of the aneurysm or of the aorta above the aneurysm; the ligament of Treitz was incised so that the aorta could be exposed beneath the pancreas as far as the renal arteries. The posterior parietal peritoneum was incised from this point down over the aneurysm and beyond the aortic bifurcation. The right and left ureters were isolated and preserved. On occasions, one or the other ureter was involved in the wall of the aortic aneurysm and had to be dissected from it. The inferior mesenteric vein likewise often had to be dissected away from the aneurysmal wall but could

1. Grindlay, J. H., and Waugh, J. M.: Plastic Sponge Which Acts as a Framework for Living Tissue: Experimental Studies and Preliminary Report of Use to Reinforce Abdominal Aneurysms, A. M. A. Arch. Surg. **63**:288-297 (Sept.) 1951.

2. Wylie, E. J.; Kerr, E., and Davies, O.: Experimental and Clinical Experiences With the Use of Fascia Lata Applied as a Graft About Major Arteries After Thrombo-Endarterectomy and Aneurysmorrhaphy, Surg., Gynec. & Obst. **93**:257-272 (Sept.) 1951.

usually be preserved. The inferior mesenteric artery in each case was ligated and divided close to its origin from the aorta without ill effects. The most tedious part of the dissection was the separation of the right wall of the aneurysm from the inferior vena cava and from the left common iliac vein. This was done by

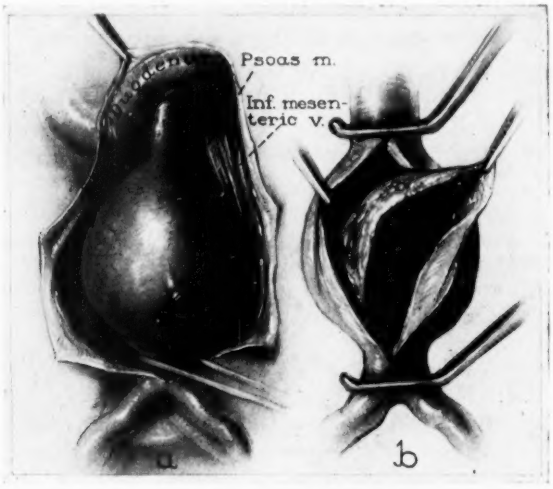

Fig. 2.—*a*, Isolation of the aneurysm. *b*, Thromboendarterectomy begun by removal of clot, intima, and portion of media after the aorta is clamped.

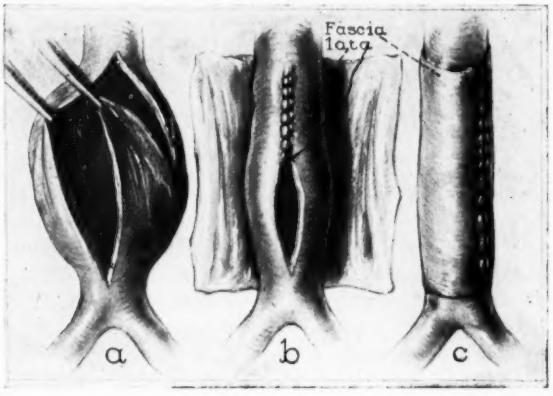

Fig. 3.—*a*, Trimming of outer shell of aneurysm. *b*, Reconstruction of normal-sized tube. *c*, Wrapping of aorta with fascia lata.

sharp dissection, for attempts at blunt dissection usually resulted in tears in the inferior vena cava. Finally, tapes were passed around the aorta above and below the aneurysm, which was then separated from the lumbar veins and vertebral column posteriorly. During the course of this procedure several pairs of lumbar arteries were ligated and divided.

After complete mobilization, appropriate clamps were placed on the aorta above and below the aneurysm. An incision was made in the anterior wall of the aorta from a point just above the aneurysm down across it to the aorta or the iliac arteries below. Thromboendarterectomy was done through this incision, with removal of the large mass of thrombus together with the calcified intima and the inner portion of the media (Fig. 2). The remaining outer wall of the aortic aneurysm was trimmed down so as to form an essentially normal-sized tube (Fig. 3*a*). This was closed with two rows of 00000 continuous nonabsorbable surgical (silk) sutures, after the lumen was filled with a solution of heparin

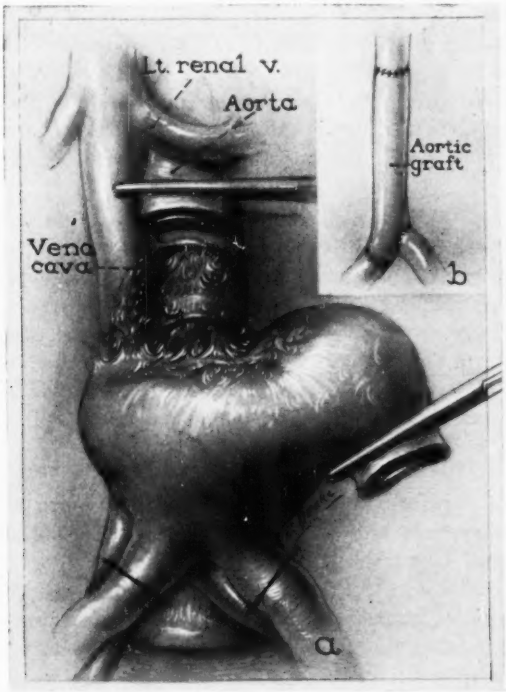

Fig. 4.—*a*, Mobilization of aneurysm after transection of aorta. *b*, Graft in place after resection of aneurysm.

(Fig. 3*b*). A piece of fascia lata, previously removed from the thigh, was wrapped snugly around the aorta and sutured into place (Fig. 3*c*). In the last two patients, this was further reinforced by wrapping with polyvinyl sponge. After removal of the clamps, the posterior parietal peritoneum was sutured together over the operative site.

In the last three patients, bilateral lumbar sympathectomy was done after completion of the aortic mobilization and before the aorta was clamped. A total of four patients in our series were treated by means of thromboendarterectomy.

Resection and Replacement by Aortic Graft.— The technique for resection of arteriosclerotic aneurysms of the abdominal aorta and their replacement by grafts

of preserved aorta has been developed by Dubost and his associates,[3] Schafer and Hardin,[4] and others. The initial dissection and exposure in the one case in which we used this method was as described for the thromboendarterectomy; however, the difficult phase of the dissection, namely the separation of the aneurysm from the inferior vena cava and the left common iliac vein, was deferred until clamps were placed proximal and distal to the aneurysm. The aorta was then transected just beyond the proximal clamp and peeled down out of its bed by means of sharp dissection. This allowed good exposure of the difficult parts of the dissection posteriorly and along the inferior vena cava (Fig. 4*a*) .The common iliac arteries were severed just distal to the aneurysm, appropriate clamps having been placed on them. The segment of aorta containing the aneurysm was resected, and a preserved homologous graft from the upper part of the descending aorta was sutured into place (Fig. 4*b*). The technique of Dubost and his group[3] was used. It is surprising, but true, that a satisfactory union can be made between the extremely sclerotic aorta of the recipient and the pliable elastic aorta of the donor. Again, bilateral lumbar sympathectomy was done just before the aorta was clamped.

Reinforcement with Polyvinyl Sponge.—Eighteen patients in our series were treated by reinforcement with polyvinyl sponge. As performed in this series, the operation of reinforcement of abdominal aneurysms with this material is not an extensive procedure. In most cases, no attempt was made to separate the aneurysm from the vena cava or to mobilize it posteriorly, for in this operation little chance exists to reinforce or control any tears made into the aorta during dissection. Thin plaques of polyvinyl sponge were laid against all the exposed surfaces of the aneurysm and carefully sutured into place.

OPERATIVE MORBIDITY AND MORTALITY

Among the 18 patients who were treated by means of reinforcement of the abdominal aortic aneurysm with polyvinyl sponge, two died during the immediate postoperative period. One of these deaths occurred on the 17th postoperative day as the result of renal failure; the other was caused by massive thrombotic occlusion of the iliac arteries immediately after operation, necessitating a second operation about 10 hours after the first. The patient died 24 hours later. No other instances of disturbance of the arterial supply to the legs were encountered as a result of this procedure.

One of the four patients in whom thromboendarterectomy was performed died in the immediate postoperative period. This patient had a huge aneurysm involving the right common iliac artery that was leaking and causing constant severe pain in the right lower quadrant at the time of operation. Diffuse arteriosclerosis was present in the abdominal aorta and iliac vessels. Although difficult, the procedure of mobilization, thromboendarterectomy, and bilateral lumbar sympathectomy proceeded satisfactorily. After operation the supply of arterial blood to the right

3. Dubost, C.; Allary, M., and Oeconomos: Anéurysme de l'aorte abdominale traité par resection et greffe, Arch. mal. cœur **44**:848-851 (Sept.) 1951.

4. Schafer, P. W., and Hardin, C. A.: The Use of Temporary Polythene Shunts to Permit Occlusion, Resection, and Frozen Homologous Graft Replacement of Vital Vessel Segments: A Laboratory and Clinical Study, Surgery **31**:186-199 (Feb.) 1952.

leg was excellent and continued so throughout the seven days that the patient lived. Arterial insufficiency developed rapidly in the left leg opposite the side operated on; gangrene was apparent at the time of the patient's death from cardiac failure on the eighth postoperative day. At necropsy the left common and external iliac arteries were nearly completely occluded by thrombi. The right common iliac artery, the site of the thromboendarterectomy, had a good lumen, and no evidence of further aneurysmal formation was present.

Of the three patients who survived the operation of thromboendarterectomy, two had uncomplicated convalescences. In the third, the first patient in this series in whom this operation was done, arterial insufficiency developed in the left leg in the early part of the postoperative period, necessitating a midthigh amputation on that side. Two factors probably contributed to this difficulty. Bilateral lumbar sympathectomy was not done in this patient but was done in subsequent patients. Also, a retrograde aortogram had been attempted through the left common femoral

TABLE 1.—*Operative Mortality in Arteriosclerotic Abdominal Aortic Aneurysms*

Procedure	Cases, No.	Deaths	
		No.	Per Cent
Reinforcement with Ivalon sponge	18	2	11
Thromboendarterectomy	4	1	25
Resection and grafting	1	0	0

TABLE. 2.—*Survival after Operation for Arteriosclerotic Abdominal Aortic Aneurysm*

Procedure	Cases, No.*	Death Within Two Years	
		No.	Per Cent
Reinforcement with Ivalon sponge	15	5	33.3
Thromboendarterectomy	3	1	33.3

* Includes only operations prior to Jan. 1, 1953; deaths in immediate postoperative period not included.

artery about a week prior to the definitive operation. After this, the pulsations of the major vessels of the left leg were greatly diminished, although no other evidence of arterial insufficiency was present. All subsequent aortograms have been done by means of the translumbar method of injection.

The patient who was treated by resection of the aneurysm and replacement by an aortic homograft had a satisfactory convalescence. Pulses were normal in both legs at all times. The operative mortality is summarized in Table 1.

RESULTS OF OPERATION

Reinforcement With Polyvinyl Sponge.—Follow-up studies were done in 15 patients treated by reinforcement of the abdominal aneurysm with polyvinyl sponge; the longest follow-up period was two years, the shortest two and a half months. Within this period, five patients (33.3%) had died as a result of the disease (Table 2), and a sixth patient, although still alive, suffered from constant, severe, and progressing pain. Thus, six patients (40%) presented evidence of continuing extension of the aneurysm in spite of treatment. The histories of death in each of the five patients were typical of rupture of a large abdominal vessel, presumably the aorta; this was substantiated in two instances by necropsies, one at home

and one at the clinic. Although our information is not complete, the available data suggest that the rupture had occurred in regions other than those reinforced by the sponge.

The remaining nine patients treated by reinforcement are alive and without pain. Four of these nine patients had severe abdominal pain, either steady or episodic, prior to operation. It is possible that mobilization of the posterior parietal peritoneum, duodenum, ureters, and other organs from the expanding surface of the aneurysm gives palliation of pain in some instances.

Thromboendarterectomy.—The three patients who survived the operation of thromboendarterectomy were operated on 14, 13, and 8 months, respectively, prior to the follow-up. Two of these patients are alive and asymptomatic, while one, operated on 13 months before the follow-up, died suddenly seven months after operation. Thus, in this short period, one of three patients surviving thromboendarterectomy has died, presumably of aortic rupture (Table 2). One of the two survivors was without symptoms prior to operation; the second was operated on during acute leakage of the aneurysm and had experienced constant severe abdominal pain.

TABLE 3.—*Death from Abdominal Aortic Aneurysms After the Time of Diagnosis* *

Period, Yr.	Traced Patients Dead at End of Indicated Period, %
1	33
2	42
3	51
5	81

* Modified from Estes.[5]

Resection and Graft.—The patient treated by resection of the aneurysm and replacement by a graft of preserved aorta has not been followed for a sufficient length of time to allow any conclusions as to prolongation of life.

COMMENT

In order for meaning to be attached to survival rates in patients operated on because of arteriosclerotic aneurysms of the abdominal aorta, such figures must be compared with rates in patients who have untreated aneurysms. Estes [5] observed that 33% of patients who had arteriosclerotic aneurysms of the abdominal aorta died within a year of diagnosis; another 17% died by the end of three years. Thus, approximately half of such patients were dead within three years of the date of diagnosis (Table 3). The majority of these patients died of rupture of the aortic aneurysms. To be of value, any operative procedure for the treatment of aortic aneurysms must result in an improved survival rate or in great relief of symptoms. Even saving a patient from an acute episode of aneurysmal leakage cannot be construed as certain evidence of the efficacy of the procedure, because, occasionally, patients have recovered spontaneously from such leakages and have lived for three or four years.[5]

5. Estes, J. E., Jr.: Abdominal Aortic Aneurysm: A Study of 102 Cases, Circulation **2**:258-264 (Aug.) 1950.

No suggestion of a higher survival rate in the treated group can be found when the results in our series of patients who were treated by reinforcement with polyvinyl sponge are compared with results in the series of untreated patients reported by Estes. Similarly, when the results in the admittedly small group of patients treated by thromboendarterectomy are compared with those of the control group, no suggestion appears of a greater percentage of survivals in the group operated on. Cognizance is taken of the small number of cases in the treated group and of the relatively short period of observation; however, the trends appear to be significant.

No sufficiently large series of cases has been published to allow final evaluation of many of the methods utilized in the treatment of these abdominal aortic aneurysms, both as to technical problems and as to their efficacy in prolongation of life. Certain tentative conclusions must be drawn, however, in order that physicians may treat patients who have this fatal disease in a manner that appears most hopeful of alleviating suffering and producing a cure.

Partial proximal ligation has been attempted sporadically as a definitive method of treatment. We are aware of no report that establishes the efficacy of this procedure.

Introduction of long lengths of wire into these aneurysms, either alone or associated with electrothermic coagulation, would appear to have theoretic merit. Yet, published results to date of the "pack" method of wiring [6] have failed to demonstrate prolongation of life greater than that noted in comparable control patients. The results from partial proximal ligation combined with wiring and electrothermic coagulation, published by Blakemore,[7] are encouraging but do not as yet clearly demonstrate a greater percentage of survivors for a significant period than is found in control series.

Reinforcement of aneurysms by Cellophane,[8] cutis grafts,[9] polyvinyl sponge, and other materials [10] is an appealing approach to the treatment of these lesions because the procedures are relatively simple and produce little risk to the patient; however, our early experience would suggest that reinforcement with polyvinyl sponge is of questionable value in the prolongation of life but has afforded relief of pain in some patients.

The actual wrapping of an aneurysm with any substance, such as cutis grafts or Cellophane, demands complete mobilization of the aneurysm. This complete mobilization appears to be more difficult technically and is probably more hazardous than the procedures of resection and grafting. So few cases in which complete mobilization and wrapping have been accomplished are reported in the literature that no conclusions can be drawn as to the value of this technique.

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6. Linton, R. R.: Intrasaccular Wiring of Abdominalarteriosclerotic Aortic Aneurysms by the "Pack" Method, Angiology **2**:485-498 (Dec.) 1951.

7. Blakemore, A. H.: Progressive Constrictive Occlusion of the Abdominal Aorta With Wiring and Electrothermic Coagulation: A One-Stage Operation for Arteriosclerotic Aneurysms of the Abdominal Aorta, Ann. Surg. **133**:447-462 (April) 1951.

8. Poppe, J. K.: Cellophane Treatment of Syphilitic Aneurysms With Report of Results in 6 Cases, Am. Heart J. **36**:252-256 (Aug.) 1948.

9. Lowenberg, E. L.: Aneurysm of the Abdominal Aorta: Report of 2 Cases Treated by "Cutis Grafting," Angiology **1**:396-404 (Oct.) 1950.

10. Berman, J. K., and Hull, J. E.: The Treatment of Aneurysms With Fibroblastic Agents: Experimental and Clinical Studies With the Use of Sodium Dicetyl Phosphate, Surg., Gynec. & Obst. **94**:543-549 (May) 1952.

At first glance the operation of thromboendarterectomy was appealing, since it removed a considerable portion of the aneurysm and reconstructed a normal-sized vascular channel. In an extremely limited experience, however, our early hopes as to the efficacy of this procedure have not been entirely fulfilled. Furthermore, the operation is troublesome in that mobilization of the aneurysm posteriorly and from the vena cava is made exceedingly difficult by the large size of the aneurysm. Difficulty is encountered also in being certain that the fascial wrapping covers the entire region from which intima and media have been removed; thus, the risk of a late blowout is courted.

In both thromboendarterectomy and grafting, cross clamping of the abdominal aorta just below the renal arteries is necessary. We have, as have others, occluded the aorta in this region for periods as long as 1 hour 45 minutes; usually no ill effects have occurred. Although we do not know whether this can be done in large numbers of cases without loss of limb or without immediate cardiovascular disturbances, it is our opinion at the moment that such occlusions generally are well tolerated provided that an excellent flow is restored through the operative site and into the legs when the occlusion is released. As yet, insufficient experience has accumulated to allow final evaluation of this risk; also, it is not known whether temporary bypassing of the operative site by means of mechanical shunts [11] is of value in minimizing complications.

A great technical advantage of excision of the aneurysm and its replacement by an aortic graft lies in the fact that after placement of appropriate clamps the aorta can be transected just proximal to the upper limits of the aneurysm. As emphasized to us in a personal communication by Bahnson, the aneurysm can then be turned down and dissected out of its bed under direct vision, much as the gall bladder is dissected out of its fossa after its pedicle is secured. It appears that by this method a great percentage of these aneurysms can be mobilized even when they are intimately associated with the vena cava or actively leaking. Anastomosis between the graft and the sclerotic aorta can be effected. Some late disruptions of these lines of suture may occur; only time and further experience will determine this. The arteriosclerotic aorta above or below the operative site may weaken subsequently and allow further formation of aneurysms. Finally, the fate of the grafts themselves is not entirely clear. Evidence is present that some undergo calcification and dilatation.[12] The results to date, however, give encouragement as to their continued use. Obviously, questions are yet to be answered as to the fate of patients who are treated by resection of aneurysms and replacement by grafts, but the merits of this method warrant further trial.

In certain cases, no doubt, the condition is not amenable to this form of treatment. Patients who have multiple arteriosclerotic aneurysms in the thoracic and abdominal aorta, those who have extreme dilatation of the aorta above the aneurysm, and those who have severe systemic disease probably will be in such a category. Admittedly, resection and replacement by a graft is an operation of considerable

11. Clatworthy, H. W., Jr., and Varco, R. L.: A Small Bore Polythene Shunt to Prevent Mechanical Shock After Prolonged Cross-Clamping Thoracic Aorta, Proc. Soc. Exper. Biol. & Med. **74**:434-436 (June) 1950. Schafer and Hardin.[4]

12. Gross, R. E.: Treatment of Certain Aortic Coarctations by Homologous Grafts: A Report of 19 Cases, Ann. Surg. **134**:753-768 (Oct.) 1951.

magnitude; however, it must be recalled that 50% of patients who have untreated arteriosclerotic aneurysms are dead within three years of the time the diagnosis is made; most of these die of rupture of the aneurysms.

CONCLUSIONS

Thus far, the over-all results, in our hands, of the treatment of arteriosclerotic aneurysms by reinforcement with polyvinyl sponge or by thromboendarterectomy have been disappointing. However, the former operation has provided relief of pain in 44% of the survivors.

Resection and replacement by a preserved homologous aortic graft was used in the treatment of one patient with excellent immediate results. Final evaluation of this procedure will require comparison of results in a larger series of such cases with results in an untreated control series.

ADDENDUM

Since preparation of this paper, resection of aneurysms and replacement by preserved grafts have been done in four additional cases without death.

ABSTRACT OF DISCUSSION

DR. ARTHUR H. BLAKEMORE, New York: Over the 10-year period from 1943 through 1952, my colleagues and I have operated upon 84 patients with arteriosclerotic aneurysms of the abdominal aorta.

The electrothermic method of wiring aneurysms was employed as the basic procedure in the great majority of the cases. In many cases the operation was done in stages—the second stage, to achieve complete clotting of the aneurysm with diversion of blood flow into preformed collateral channels.

In July, 1948, the abdominal aorta in a 33-year-old woman was banded to the size of a cigarette, employing slingshot rubber encased with polyethylene diacetyl phosphate film. This resulted in complete closure of the abdominal aorta within the seven-month period. Starting in 1949 and through 1952 this method of banding the aorta was employed in conjunction with wiring and electrothermic coagulation in the treatment of 32 patients with arteriosclerotic aneurysms of the abdominal aorta. The ages of the patient ranged from 51 to 78 years.

There were seven postoperative deaths in the series; necropsies were obtained in all. Death was not unexpected in four patients who were operated upon for the control of hemorrhage due to rupture of their aneurysms. The mortality rate in the remaining 28 cases was 10.7%.

Of the 25 patients followed 10 are dead: 4 died of rupture of the aneurysm; 3 of myocardial infarction; 1 of rupture of a cerebral artery; 1 of carcinoma of the prostate, and 1 of pneumonitis. The survival periods ranged from one month to three years.

Analysis of the patients who died of rupture of their aneurysms is as follows: Complete restoration of blood flow in the aorta occurred in one patient; the band had necrosed through the aorta wall and passed distalward into the aneurysm without the occurrence of hemorrhage at the band site. The patient died 10 months later of rupture of the aneurysm into the transverse colon. Four layers of plastic film were employed to wrap the rubber band in this case. In all patients operated upon subsequently, 16 to 20 layers were used. Almost complete restoration of the full diameter of the aorta occurred in a second patient in whom the aneurysm ruptured seven months after operation. In this patient we had employed one thickness of a synthetic rubber band, and the mattress sutures pulled out. Since that time we have employed double-thickness gum rubber in all patients. A postoperative aortogram in a third patient with a ruptured aneurysm revealed what, in the light of our increased experience with banding, amounted to too little constriction of the aorta. Jet strain upon the aneurysm resulted. Had a second-stage wiring been done, clotting the aneurysm completely and thus diverting all the aortic blood flow through the collateral vessels, these three patients might have been saved.

In the fourth patient with rupture of the aneurysm, we are prepared to accept the interpretation that rupture may have occurred at the band site, which in this case encircled the upper pole of a very large aneurysm that extended right up to the renal arteries. Unfortunately, no necropsy was obtained. If we were treating this man now we would wrap the aneurysm up with Vinyon-N plastic cloth before placing the constrictive rubber band.

The longest follow-up period for the 15 patients who are living is four years; the shortest 9 months.

A second-stage operation for completing the closure of the aorta has been performed in 4 of the 15 patients.

In three patients the aorta subsequently became completely occluded, much as occurred in the 33-year-old woman. In confirmation of the safety of the electrothermic method of wiring aneurysms, there was but one instance of loss of tissue from anemic necrosis, and this occurred in the distal phalanx of a toe.

For additional support to the aneurysm sac, we are now employing Vinyon-N cloth on the outside of the aneurysm.

In conclusion we may state that our experience in 84 cases of arteriosclerotic aneurysms of the abdominal aorta has taught us that we may expect cure of an aneurysm that is completely clotted with diversion of the aortic blood flow through the collaterals. Recent experience with the combined procedure of wiring and electrothermic coagulation, banding the aorta to a diameter of 5 to 7 mm., and application of Vinyon-N cloth around the aneurysm would indicate that we may expect stabilization of the aneurysm with maintenance of adequate aortic blood flow.

Dr. Geza de Takats, Chicago, Illinois: I can summarize our experience with the treatment of abdominal aneurysms by showing a few slides. In this way I think we can cover the subject much faster.

[Slide] I am embarrassed to say in contradiction to Dr. Blakemore, who first became interested in this subject by 1943, that we started wiring thoracic aneurysms in the early 1930's. That, of course, dates me very definitely.

As you know, the normal treatment of aneurysms has not changed, but the character of the aneurysms has changed a great deal. At least, in the Middle West we see very few thoracic aneurysms, and what we are dealing with now, primarily, in most vascular clinics, are sclerotic aortic aneurysms. This is the reason that the wiring procedures which we have used—and of course, the method is a good 100 years old, if not more—are not so well applicable in our experience with abdominal aneurysms.

We have wired 35 aneurysms in the thorax and 10 in the abdomen. In 50% of these cases the results were considered failures; in the other half, we achieved what we felt was an arrest of the disease. By that we mean that there was pain relief, and the lesion was stationary. However, all of the patients died within three to five years, which, as I understand from the Mayo Clinic statistics, is the average life expectancy.

Then we began to wrap the aneurysm in Cellophane with strips; later Dr. Blakemore suggested the use of constricting rubber bands under which Cellophane was placed. A combination of these measures was also employed, namely, wiring, intercellular wiring, proximal constriction, and Cellophane.

I must say we have difficulty with the proper amount of constriction. Dr. Blakemore pointed out that it is extremely difficult to constrict down to just the optimal level. If there is not enough constriction, a split results. If there is too much constriction, a sudden closure might occur, which could mean, particularly if the circulation is unprepared, that the amount of constriction is not satisfactory.

We also tried using phosphate on two aneurysms, but our animal experiments on rabbit aortas have not been too convincing. We were unable to get consistent constriction of rabbit aortas after they had been sprayed with diacetyl phosphate.

[Slide] Now, we had attempted in one case the operation which Dr. Kirklin proposed, but we were unable to complete it, and we do not believe in it on the basis of our present experience—I believe it is also the opinion now that this operation should be abandoned—and we have done one partial resection of the aorta which held for three months and then ruptured.

In addition to these two patients in our service, Dr. Julian resected the aneurysms and replaced them with Y-shaped arterial grafts. There is no question in my mind that that is the optimal procedure.

I believe it is necessary to differentiate here between optimal procedures and feasible procedures. I agree completely with Dr. Kirklin that the optimal procedure is resection of the aneurysm and replacement with a Y-shaped frozen preserved graft.

But there are a number of patients who will not tolerate six-to eight-hour operations. The crux of the problem is, to my mind, the palliative procedure with which we have struggled for over 20 years, namely, that wiring, wrapping in Cellophane, partial constriction, and then combinations of these operations are worth while. They are feasible procedures.

Mortality with these operations so far has been zero, but like Dr. Kirklin, we have not been convinced that these measures have actually delayed rupture.

All of these operations accomplish one thing. They relieve pain, and, although I am not certain of this, I have a feeling that the splitting of the posterior peritoneum and the decrease of lateral tension on the wall is sufficient to stop pain. None of these aneurysms, as has been pointed out by Dr. Blakemore, ever produce an erosion of the aorta. They may renew the spinal column, but pain in the abdomen and the aneursym come from lateral tension from the peritoneum.

If one wishes to relieve pain, explore the aneurysm and split the peritoneum.

Rupture of the aneurysm takes place most frequently into the parietal peritoneum fossa, and of course, rupture invariably is followed by death.

DR. HENRY BAHNSON, Baltimore: Most of the points I had intended to make have been made by Dr. Kirklin and previous discussors. I should like to compliment Dr. Kirklin on this presentation and to agree with him that the treatment of choice is resection and substitution by a homograft.

The points I had intended to make and should like to reemphasize are that many aneurysms have as their weakest point areas which are replaced posteriorly. If one can remove or reinforce them, one can expect a good result; if not, such a result is not to be expected.

I should like to show just the last slide if I may.

The slide summarizes the work that we have done in excising the arteriosclerotic aneurysms. I should like to emphasize a point Dr. deTakats made.

The arterial aneurysms occur in the terminal aorta, and it has been striking that in the 12 patients we have operated upon in the last year all had aneurysms which were located below the renal arteries.

I know we will encounter some that go higher. In all instances we have been able to occlude the aorta between the renal arteries and the upper edge of the aneurysm and to remove it.

[Slide] This is a summary of the 12 patients we have treated. The one patient shown here was treated by endarterectomy.

This is the procedure, and it is not nearly as satisfactory as resection and replacement by a homograft. We have used grafts in 10 patients. Four of these grafts were placed between the proximal aorta and the distal aorta, and others were used in arrangements between the aorta proximally and the external iliac distally.

In this one instance we used the procedure Dr. Kirklin described of anastomosing to the side of aorta graft. This patient was the one patient who died in the group. He had an aneurysm which had ruptured. He was in shock when the procedure was begun and died before the aneurysm could be excised.

I should like to emphasize that this is not a selected group of patients. No operation has been refused a patient because of too extensive disease, either due to local arteriosclerosis, or general arteriosclerosis, or other disease.

In this group one patient was 78 years old. In one patient with previous coronary thrombosis the systolic blood pressure was 220 mm. Hg; another patient had previously treated cardiac failure and pulmonary edema.

All these patients had known disease in the adjacent vessels. An anastomosis of the diseased aorta and iliac vessels had not been as difficult as we had expected, and we have been able to accomplish it without significant leak in all instances.

We know we are operating upon elderly patients with arteriosclerosis. We feel we are treating the most dangerous form of this disease. In those patients with abdominal pain, this pain is itself an important indication for operation.

We have encountered one significant complication. This occurred in a 70-year-old man with a great deal of abdominal pain and an apparently recently formed aneurysm due to dislodging some of the clot or to extension of peripheral vascular disease, I do not know which, but he lost portions of both legs.

The other 10 patients are either well or convalescing from fairly recent procedures.

DR. MICHAEL DE BAKEY, Houston, Texas: I want to say first that I, too, agree with the general thesis that has come out of this discussion, that the most effective approach to this problem now seems to be resection and replacement of the segment by an aortic homograft.

Our experience with this procedure in this type of aneurysm includes 13 cases, with 1 death. This death occurred in a 75-year-old woman who had severe impairment of renal function and was in a state of partial uremia at the time of operation.

Operation was advised because of apparent rupture of aneurysm. She died on the 13th postoperative day of progressive uremia. All the other patients have done extremely well, considering the fact that the majority are in the older age group.

Eleven of the patients were over 60 years of age, and two were over 70.

Like Dr. Bahnson, we have not declined operation in any of the cases. They represent a consecutive series, and in many instances the condition was very extensive in nature.

In all cases in which operation was done, the procedure was technically carried out successfully, although, as I said before, one of the patients died in the postoperative period.

[Slide] May I have the slides? I should like to show these rather hurriedly. Some of the points have already been made.

This is the exposure we use.

[Slide] This is the procedure of replacement by the aortic homograft. This is merely to illustrate the extensive nature of some of these aneurysms.

You will note this patient has not only a huge aneurysm of the abdominal aorta itself, but also another large aneurysm of the iliac on the right side, and another aneurysm on the left side. It is possible to resect all three and place that segment with aortic homograft as shown here.

[Slide] This slide and the next slides will illustrate the point which I think is worthy of emphasis. This is a patient on whom the so-called Cellophane-wrapping procedure had previously been done, approximately eight months ago. This is the resected specimen when the patient had the most recent operation with resection and replacement by graft.

The aneurysm had been split open, and you will note the lumen of the aneurysm, laminated clot. This is the external wall, and between this is the degenerated laminated clot; this is the portion poured out.

You can see some of the grey dirty portion of the clot and the thin wall on the outside.

This aneurysm had been wrapped on the outside with Cellophane.

The point I wish to make is that there is a tendency to use Cellophane. Diacetyl phosphate film, or any other type of foreign material which wraps around the aneurysm, then separates the wall of that aneurysm from its possible vascularization. The aneurysm becomes a relatively isolated wall between the clot and the outside which is in approximation with the film.

The result is a tendency for further devascularization of the wall. This gives you some idea of why the rupture takes place. The rupture is really the result of pressure necrosis of the clot and devascularization of the wall.

[Slide] The next slide shows the histologic section of such an aneurysm. This is the Cellophane film and here is the aneurysmal wall with degenerative clot and the relatively thin portion of fibrosis that has occurred around it, obviously inadequate to support the aneurysm.

Here is the result of treatment of an aneurysm by partial ligation, usually with a rubber tube wrapped with film. Now the necrosis has taken place in that, with the rubber apparent in the wall of the aneurysm. This is the resected specimen.

As a result of our experience with five cases of aneurysms that have previously been wrapped with Cellophane and subsequently resected, the intervals varying between 8 and 42 months, we are convinced that use of the so-called Cellophane-wrapping procedure or any other procedure of wrapping is not only ineffective but probably harmful.

MALIGNANT GANGLIONEUROMA OF THE GANGLION NODOSUM OF THE VAGUS NERVE

GEORGE T. PACK, M.D.
IRVING M. ARIEL, M.D.
AND
THEODORE R. MILLER, M.D.
NEW YORK

GANGLIONEUROMAS of the ganglion nodosum of the vagus nerve are extremely rare. Only two such tumors have been recorded to date.[1] A third tumor, treated by us, offered an excellent opportunity to study the nature and nosology of these neoplasms. The pertinent features of this unusual oncologic entity are presented here in detail because (1) it is the only malignant ganglioneuroma of the nodose ganglion recorded, (2) the patient is the youngest one in whom a malignant tumor of the nodose ganglion was successfully resected, and (3) the case is the only one recorded in which no permanent defect persisted after resection of a ganglioneuroma of the ganglion nodosum of the vagus nerve. The clinical and pathologic features of this neoplasm involving the nodose ganglion form the subject of this presentation.

REPORT OF A CASE

The patient was an 11½-month-old white girl, who suffered from a mass on the right side of her neck, which was first discovered when the child was 6 months of age. It was at first believed by a local physician to represent an inflammatory lymph node, but the cervical tumor grew steadily in size. An aspiration biopsy by Dr. George Erdman revealed immature neural elements; a diagnosis of cervical neuroblastoma was made on the basis of this aspiration biopsy. This diagnosis was confirmed by Dr. George Higgins. The patient was treated by her local physician with deep x-ray therapy to the cervical mass, with no diminution in its size. She received 2,000 r in air delivered in 30 days to a 6 by 8 cm. portal. The factors were as follows: 200 kv., 20 ma., 50 cm. target-skin distance, 0.5 mm. Cu and 1 mm. Al filter, and half-value layer 1 cm.

The patient was first seen by us on Nov. 5, 1952, at which time she was at the height of an erythematous reaction resulting from the irradiation. A mass 5 cm. in diameter was palpated deep in the right cervical region, with posterior fixation and without attachment to the overlying skin (Fig. 2). It was ovoid in contour and discrete. Although not attached to its contiguous structures, it was immobile because of deep fixation. A sign of interest was the anterolateral displacement of the carotid artery. The trachea was not displaced, and the patient breathed, swallowed, and cried normally.

From the Pack Medical Group.

1. (*a*) Benda, C.: Ein Fall von Ganglioneurom des Nervus vagus: Verhandl. deutsch. path. Gesellsch. **7**:266, 1904. (*b*) Clay, R. C.: Ganglioneuroma of the Nodose Ganglion of the Vagus, Ann. Surg. **132**:147, 1950.

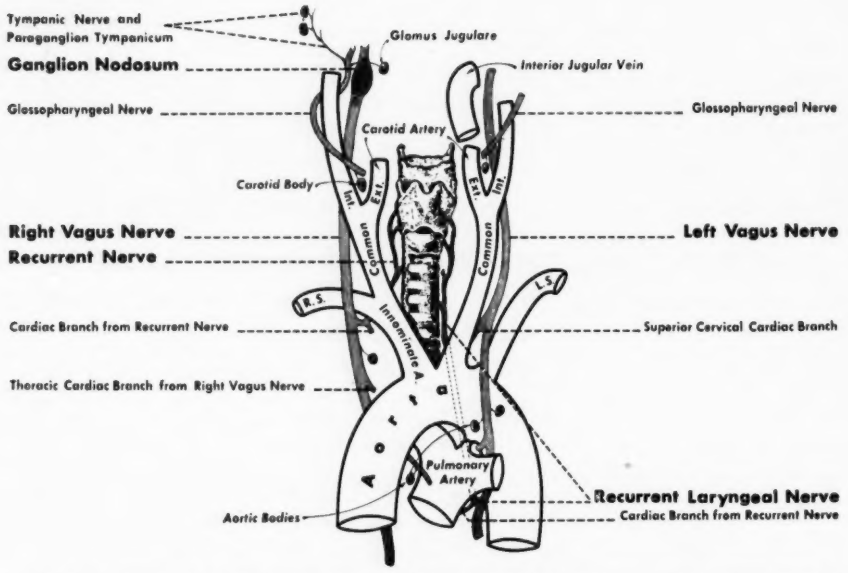

Fig. 1.—Anatomy of the vagus nerve, showing the nodose ganglion. The various ganglia and the paraganglionic structures of the parasympathetic nervous system are presented to show the sites of origin of other ganglioneuromas and paragangliomas in the cervical region.

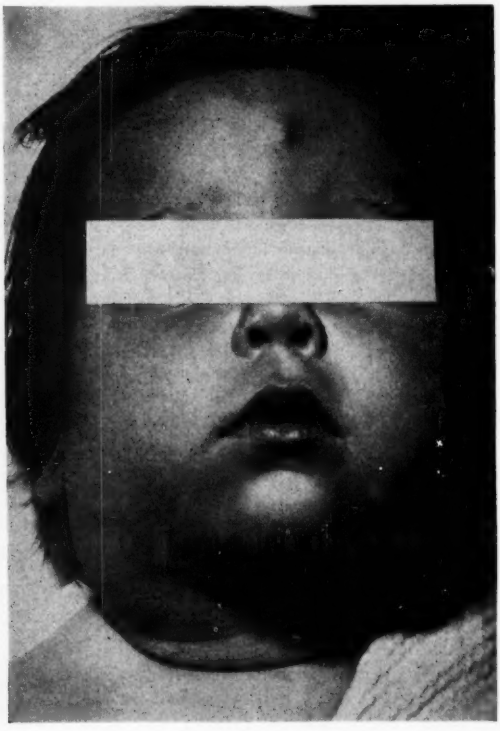

Fig. 2.—Clinical photograph of an 11-month-old child bearing a malignant ganglioneuroma of the ganglion nodosum of the right vagus nerve.

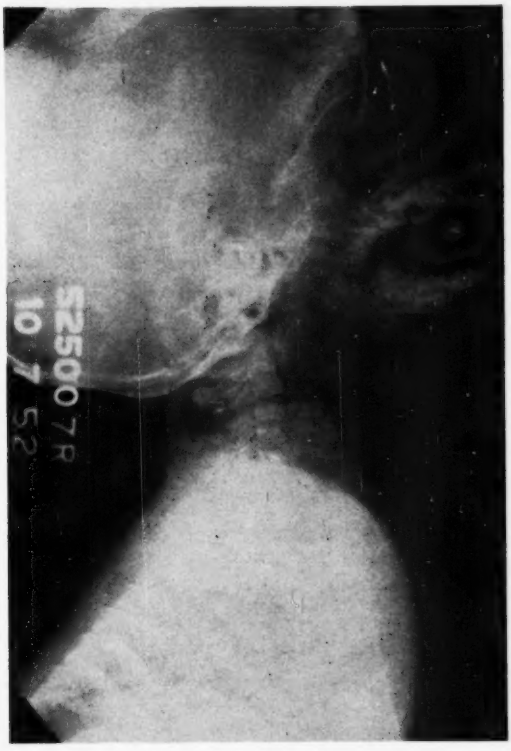

Fig. 3.—Roentgenographic appearance of the cervical malignant ganglioneuroma. Note the mottled areas of calcification scattered throughout the tumor.

Fig. 4.—Gross appearance of the ganglioneuroma, which had been dissected from the nodose ganglion of the right vagus nerve. Although histologically malignant, the tumor appears well encapsulated.

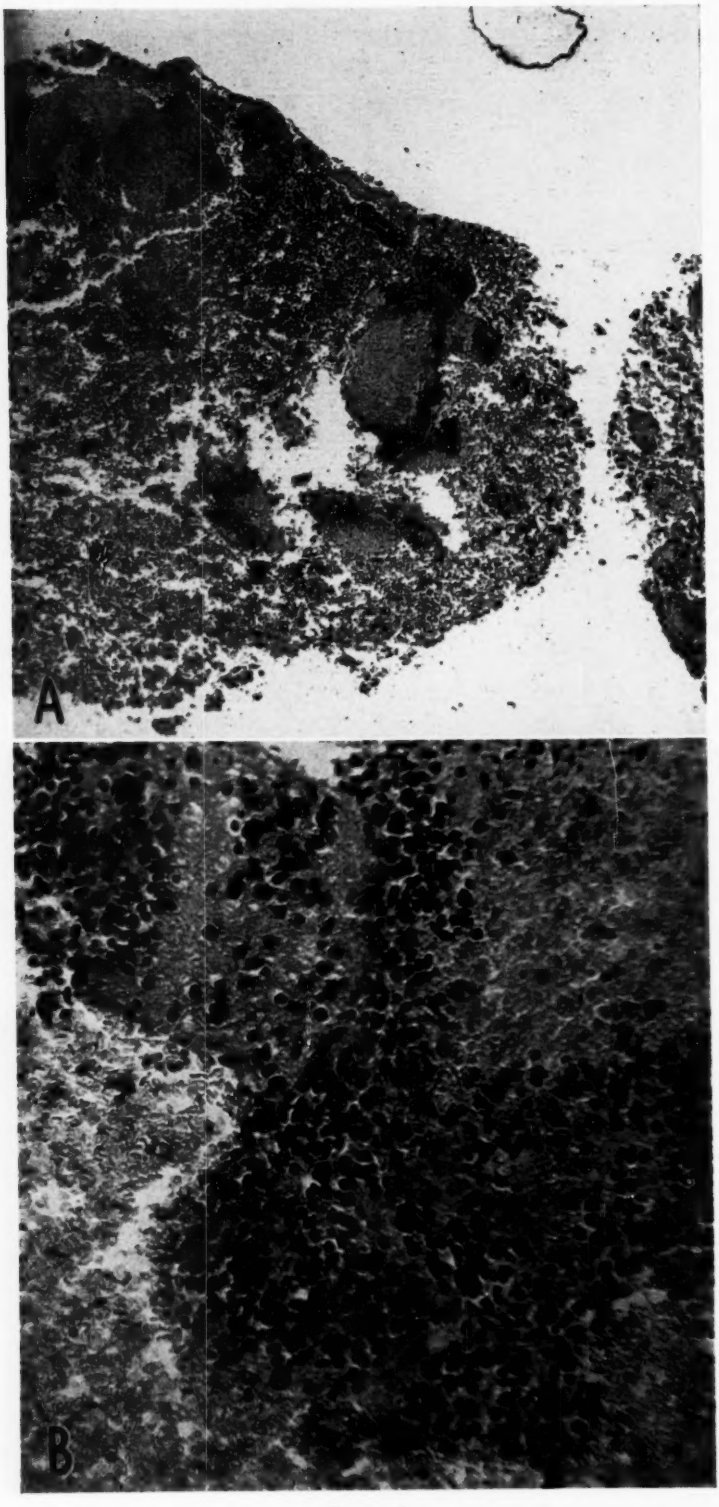

Figure 5

(See legends on opposite page)

Physical examination showed her condition was otherwise normal, except for an incidental finding of three congenital hemangiomas, one situated over the glabella, and two others on the left side of the neck. No abdominal masses were palpable, and the eyes were normal in every respect.

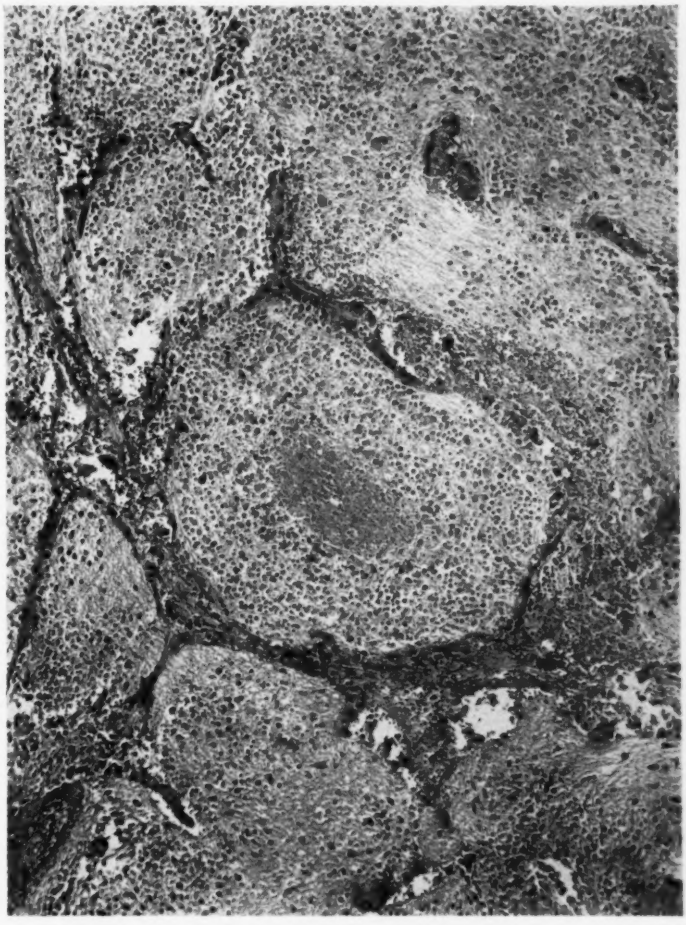

Fig. 6.—A very-low-power photomicrograph of a malignant ganglioneuroma. The lobules are separated by collagen fibers. The central regions of the lobules are frequently necrotic. There is a relative paucity of cells. The larger cells scattered throughout are ganglion cells.

EXPLANATION OF FIGURE 5

Fig. 5.—*A*, low-power photomicrograph of the aspiration biopsy specimen from the cervical tumor upon which a diagnosis of neuroblastoma was made. Foci of necrosis are located within sheets of poorly differentiated cells. *B*, higher-power magnification of *A*. Note the poorly differentiated neuroblastomatous cells, with a few more differentiated ganglionic cells interspersed throughout. Necrotic regions are seen. Courtesy of Dr. George Erdman.

Her past history was normal except that five weeks before she was seen by us she had fallen out of bed, injuring her right thigh. This injury resulted in a fracture of the distal shaft of the right femur, diagnosed by a skeletal roentgenographic survey performed at a later date. The remainder of the skeletal roentgenographs were negative for evidence of bony metastases. A roentgenogram of the cervical region revealed mottled calcification within a deep soft-tissue mass (Fig. 3).

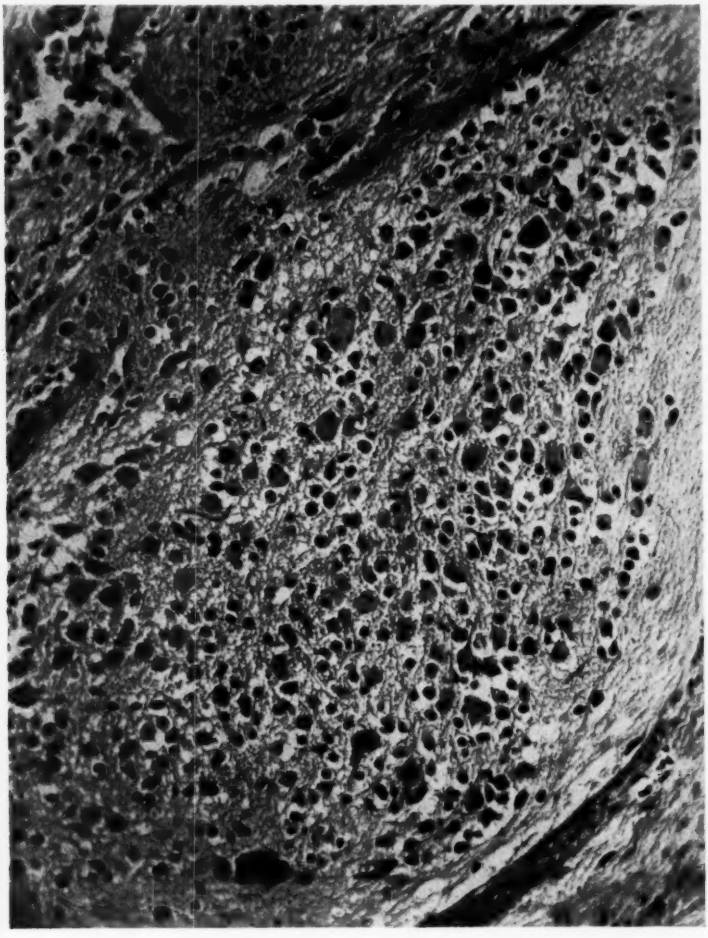

Fig. 7.—Low-power photomicrograph of one region of a malignant ganglioneuroma which consists of completely and partially differentiated ganglionic cells.

Her family history was negative for cancer. The child's birth was a full-term, normal, spontaneous delivery. Her birth weight was 6 lb. 12 oz. (3,062 gm.). Her development and growth were normal in every respect. She had no childhood diseases. Her mental development was normal.

The preoperative diagnosis was a cervical neuroblastoma. The question of whether this represented a primary neoplasm or a metastatic deposit presented itself. The rarity of cervical neuroblastomas coupled with the recent fracture of her femur might suggest this to be a

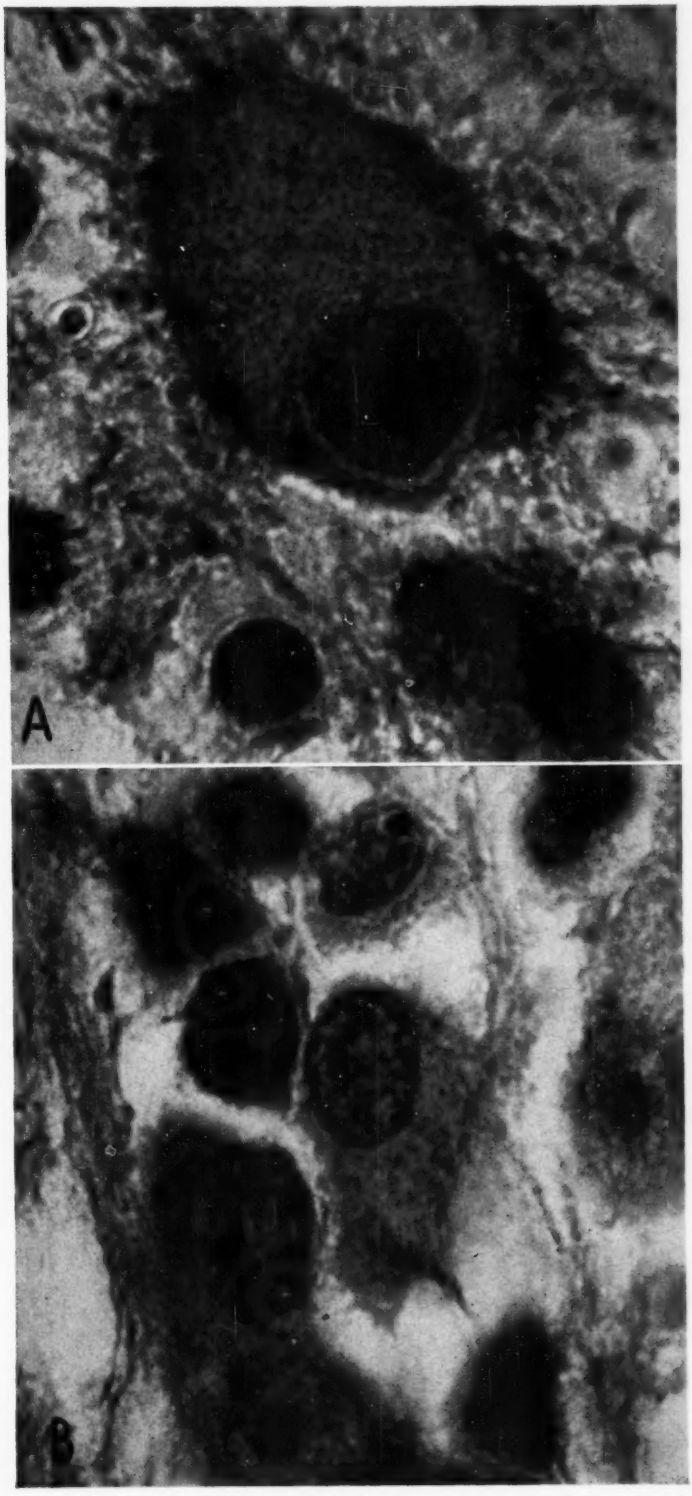

Fig. 8.—*A*, high-power photomicrograph of several cells shown in Figure 7, demonstrating differentiated ganglion cells. *B*, high-power photomicrograph of several cells shown in Figure 7, demonstrating several partially differentiated ganglion cells.

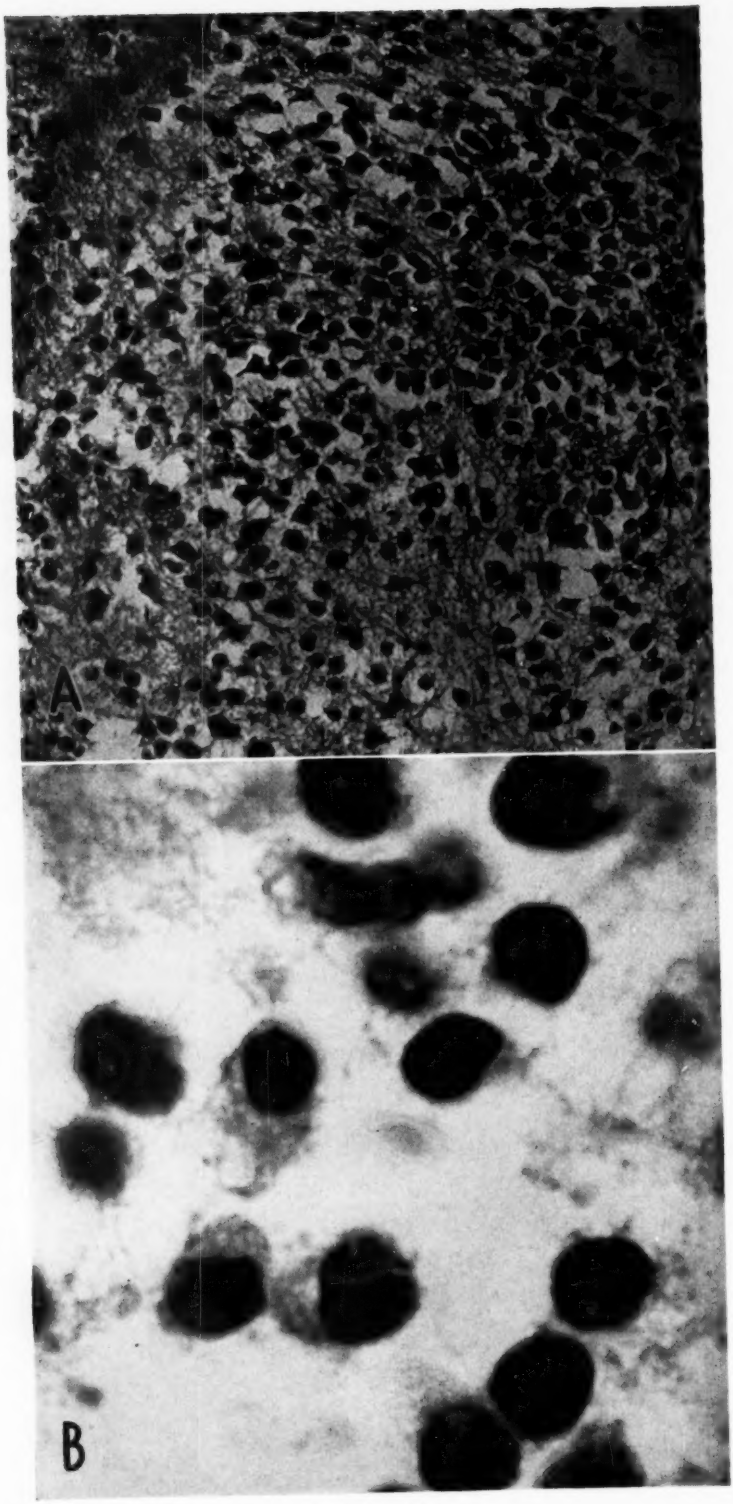

Figure 9

(See legends on opposite page)

metastasis. A roentgenogram of the femur, however, showed no osteolysis, and the fall which she had sustained was of sufficient severity to produce a traumatic fracture. The absence of any other evidence of neoplasia further indicated that the tumor was a primary one. It was accordingly decided to wait for subsidence of the erythematous radiation reaction and then to attempt surgical extirpation of this cervical neoplasm. This was successfully accomplished on Nov. 26, 1952, at the Memorial Center for Cancer and Allied Diseases. A longitudinal incision over the right sternocleidomastoid muscle with severance of this muscle permitted exposure of the neoplasm, which presented as a smooth, ovoid tumefaction measuring 5 by 3 cm., nestled within the carotid sheath. It was dissected free of contiguous tissues with difficulty, especially anteromedially, where it was attached to the vagus nerve. The right vagus nerve was pushed anteriorly, and the tumor lay posterior and lateral to the nerve, pushing it forward. The site of the tumor and its intimate relationship with the vagus nerve were identical with that of the nodose ganglion from which it originated. The carotid arteries and the jugular vein were also pushed anteriorly in front of the tumor; this made the dissection somewhat difficult. The internal carotid was attenuated and stretched over the superomedial pole of the tumor and constituted a considerable surgical hazard. The tumor compressed the vagus nerve, the glossopharyngeal nerve, and the sympathetic ganglia and nerves of this region. The superior pole of the tumor was close to the main trunk of the facial nerve, which was slightly traumatized during the dissection. By sharp dissection the tumor was dissected free and removed *in toto*. The subjacent nerves were gently compressed when the tumor was removed, but they were not particularly frayed or thinned.

Pathologic Examination.—The tumor was an ovid mass which measured 5 by 3.5 by 3.7 cm. It was reddish-brown in color, intermottled by yellowish flecks. The external surface presented a shaggy structure, composed of numerous fibrous strands. On section, the cut surface presented numerous yellowish necrotic foci intermingled with the reddish-brown surface.

Microscopic Pathology.—The following description of the histologic features of this malignant ganglioneuroma will present the appearance of structures as observed under very low magnification and proceed gradually to higher magnifications (Fig. 5). It was prepared with the cooperation of Dr. George Higgins, pathologist of the Pack Medical Group.

With the scanning lens the tumor was found to be diveded by rather coarse strands of collagen into lobulations, often incomplete, which might measure up to 1 or 2 mm., or more (Fig. 6). At the periphery these fibers intermingled with those which formed the capsule. Foci of necrosis occupied the central region of many lobules; in these, slight calcification was suggested by a faint basophilic reaction. At this magnification large ovoid and elongated cells, suggesting nerve cells and portions of neurons, were identifiable, but their number varied greatly from field to field, with no areas in which they were absent.

Increased magnification showed the resemblance of these ovoid and elongated cells to the nerve cells of the sympathetic ganglia (Fig. 7). They represented differentiated ganglion cells. Although most tended to be smaller, some reached a length of 50 μ or more. The cell body with its finely granular, pale, acidophilic cytoplasm, might assume a globular, oval, pyriform, spindle, or polygonal shape. Pointed cytoplasmic processes extended for variable distances into the surrounding areas and converged with numerous nerve fibers, which were not recognized as entities without special staining techniques. Typically, a single nucleus lay in the center of the cell. Not infrequently two, and occasionally three, were present and were located in an eccentric, or even peripheral, position. The nuclear membrane was thin and delicate. Chromatin lay in fine aggregates and was scanty, giving the cell a pale appearance unless pyknosis had developed.

EXPLANATION OF FIGURE 9

Fig. 9.—*A*, photomicrograph demonstrating a region of undifferentiated, primitive, hyperchromatic cells surrounded by a loose network of delicate nerve fibrils. Note the resemblance of this section to the original aspiration biopsy specimen. *B*, higher-power magnification of the cells shown in *A*, showing the details of the cellular structure. The cells are smaller and pleomorphic. The nucleus is large, rich in chromatin, and eccentrically placed and has a prominent nuclear membrane. The cytoplasm is scanty.

The large, prominent, dark-staining nucleolus, usually single, tended to lie in an eccentric position (Fig. 8). In the partially differentiated cells the cytoplasm was less abundant and the fibers tended to disappear. The nucleus tended to be larger, with a more prominent nuclear membrane and coarsening of the chromatin granules; the nucleolus remained prominent. As undifferentiation proceeded, the cells tended to become smaller until they approached the type characteristic of neuroblastoma. The cytoplasm became very scanty and on staining was only slightly acidophilic. The nucleus comprised most of the cell and was usually spheroidal in shape, outlined by a rather thick nuclear membrane, and dense, with a large amount of dark-staining chromatin material. Occasionally delicate neurofibrils might be seen, but they were not nearly so much in evidence as in the more differentiated regions. No pseudorosettes were seen in this specimen.

The aspiration biopsy in this patient yielded tissue which presented these histologic characteristics. A diagnosis of neuroblastoma was accordingly made on the basis of the aspirated material but was modified to malignant ganglioneuroma after the entire tumor was available for examination. There was a more or less diffuse intermingling of benign and malignant elements.

Unlike the condition in normal nerve cells, changes of senescence were evident in a larger number and were manifested by the outer rim of the cell (ectoplasm) staining more intensely and gradually developing an increasingly basophilic tinge. The nucleus stained more homogeneously, with loss of internal details, but the nucleolus remained distinct until the degenerative process was advanced. The nuclei of satellite cells (oligodendrocytes), astrocytes, etc., were seen but were not prominent in those sections stained by routine methods.

The cells lay in an acidophilic stroma composed of nerve fibers arranged densely in some areas and rather loosely in others. Although they appeared finer and shorter, and had a more diversified direction (lattice pattern) than collagenous fibers, they were most easily identified because they appeared continuous with the cell cytoplasm.

The blood vessels were not numerous and appeared prominent only in the trabeculae.

Foci of necrosis were frequent, presenting a coarsely granular appearance, and were the site of calcium deposits evident as blue granules or plates which tore the adjacent friable tissues during the preparation of the section.

Postoperative Course.—The patient's postoperative course was complicated by difficulty in breathing, due to paralysis of the laryngeal musculature; inability to swallow foods or fluids; ptosis of the right eyelid, due probably to damage of the cervical sympathetic ganglia and nerves, and right facial hemiparesis, due to surgical trauma to the facial nerve. Some of these symptoms were due to trauma to the right vagus nerve. Since none of the major nerves were severed during the operation, it was believed that the symptoms were the result of surgical manipulation of the nerves, as well as discission of some of the smaller anastomosing neurons; it was believed that the disturbances would be temporary. A tracheostomy was performed, with use of local anesthesia, on the first postoperative day because of inability to swallow and cough due to anesthesia of the hypopharynx and larynx, resulting in regurgitation, aspiration, and dyspnea. Attempts to feed the patient by an indwelling nasogastric tube were unsuccessful, as she regurgitated at sporadic intervals and continued to cough up thick mucoid secretions. Bronchopneumonia and atelectasis developed on the right side and were treated by antibiotics (penicillin and oxytetracycline [Terramycin]) and crystalline trypsin (Tryptar) aerosol into the bronchial tree through the tracheostomy tube. Her general conditioned improved, but because she remained unable to swallow, a Janeway gastrostomy, with use of local anesthesia, was performed on Dec. 10, 1952. She was discharged from the hospital on Dec. 31, 1952, and was readmitted on March 24, 1953, at which time the tracheostomy tube was removed. The facial palsy was first to disappear; later the cough reflex reappeared, and swallowing without regurgitation and aspiration became possible. The child can now breathe, swallow, and smile normally.

COMMENT

The occurrence of a malignant ganglioneuroma of the nodose ganglion of the vagus nerve has presented an opportunity to study the anatomic, pathologic, and clinical features of this rare oncologic entity. A brief discussion of tumors origin-

ating in the peripheral nerves will help toward an understanding of the position of ganglioneuromas in the classification of this group of neoplasms.

Tumors of the peripheral nerves most frequently arise from the tissues which sheathe the nerves (Schwann cells, neurilemma), and such tumors are designated as schwannoma or neurilemmoma, benign or malignant.[2] Tumors which arise from ganglia, most frequently from the sympathetic ganglia, are designated as ganglioneuroma if benign, and as neuroblastoma (sympatheticoblastoma) when malignant.[3] During embryonic development of the nervous system a group of primitive cells migrate to the dorsal surfaces of the ganglia, forming small masses and depressions of these ganglia, and these cells are therefore designated as paraganglionic cells. They may be found anywhere in the peripheral nervous system and are always associated with the sympathetic ganglion chain, which extends from the base of the skull to the coccyx. The paraganglionic cells of the adrenal glands and occasionally in other loca-

Tumors of the Peripheral Nervous System

Tissue of Origin	Benign	Malignant
1. Nerve	Amputation and traumatic neuromas Appendiceal neuromas (not neoplastic)	Neurogenic sarcoma (questionable occurrence)
2. Tissue covering nerves Cells of Schwann Neurilemma	Encapsulated neurilemmoma Plexiform (diffuse) neurilemmoma	Malignant neurilemmoma (schwannoma)
3. Nerve and neurilemma	Neurofibroma (multiple neurofibromatoses)	?
4. Ganglia	Ganglioneuroma	Sympatheticoblastoma (neuroblastoma)
5. Paraganglionic cells (sympathetic and parasympathetic systems)	Hormonally active: pheochromocytoma Adrenal medulla Retroperitoneal space Posterior mediastinum (occasionally) Hormonally inactive: paraganglioma Adrenal medulla Mediastinal and retroperitoneal ganglia Carotid and aortic bodies Glomus jugulare Ganglion nodosum of vagus nerve Ganglion in sheath of glossopharyngeal nerve (middle ear) Ciliary ganglion Argentaffin cells	Malignant pheochromocytoma
6. Aberrant central nervous system tissue	Astrocytoma (glioma) Ganglioglioma	Glioma Nasal neuroepithelioma

tions give rise to tumors designated as pheochromocytomas if hormonally active, and as paragangliomas if not hormonally active.[4] The table presents a classification of tumors which arise from the peripheral nervous system. Since the neck contains every type of nerve element presented in the table, it is possible for each type of tumor shown in the classification to occur in the cervical region. Tumors of the nerve sheaths (schwannomas) occur not infrequently in the neck, but neoplasms arising from ganglionic and paraganglionic cells are indeed infrequent.

2. Ehrlich, H. E., and Martin, H.: Schwannomas (Neurilemomas) in the Head and Neck, Surg., Gynec. & Obst. **76**:577, 1943. Murley, R. S.: A Case of Neurinoma of the Vagus Nerve in the Neck, Brit. J. Surg. **36**:101, 1948.

3. (*a*) Stout, A. P.: Tumors of the Peripheral Nervous System (Section II, Fascicle 6 of the Atlas of Tumor Pathology), Washington, D. C., Armed Forces Institute of Pathology, 1949. (*b*) Wahl, H. R.: Neuroblastoma: With a Study of a Case Illustrating the 3 Types That Arise from the Sympathetic System, J. Med. Res. **25**:205, 1914.

4. Lewis, D., and Geschickter, C. F.: Tumors of the Sympathetic Nervous System: Neuroblastoma, Paraganglioma, Ganglioneuroma, Arch. Surg. **28**:16, 1934.

The most frequent paraganglionic tumor is the carotid body paraganglioma.[5] Less frequently paragangliomas arise from the glomus jugularis,[6] the ganglion in the sheath of the glossopharyngeal nerve, and theoretically from the aortic bodies.[7] This is somewhat surprising because of the rich supply of ganglionic cells of the sympathetic nervous system and, to a less degree, of the parasympathetic nervous system (nodose ganglion of the vagus nerve, jugular ganglion, and others) which are found in this locality.

Ganglioneuromas may occasionally be found within the peripheral nerves[8] and have been described among the tumors of von Recklinghausen's disease. Most ganglioneuromas arise from retroperitoneal structures and within the posterior mediastinum. Ganglioneuromas have their origin either in sympathetic ganglia or in cells of their anlage and are found along the path of the sympathetic chain, from the base of the skull to the pelvis, including the adrenal medulla.[9] They have been reported in such anatomic regions as the tongue, spermatic cord, stomach, breast, uterus, vulva, kidney, and knee joint, arising from embryonic anlagen which have migrated. The malignant variety of this tumor, the neuroblastoma, originates most frequently in the adrenal medulla and is said to be confined almost exclusively to the sympathetic nervous system. It is usually rapidly fatal.[10] Tumors arising in the ganglionic cells in the neck (ganglioneuromas, benign and malignant) are extremely rare.[11] There have been only 16 cases of cervical ganglioneuroma recorded in the literature.[12] In 14 of these the tumor apparently arose from the sympathetic ganglia. There have been two reported cases of ganglioneuroma arising from the nodose ganglion of the vagus nerve. Benda,[1a] in 1904, reported and described a pathologic specimen of such a neoplasm obtained from an inoperable "apple-sized" mass from the right cervical region of a child who subsequently died.

5. Harrington, S. W.; Clagett, O. T., and Dockerty, M. B.: Tumors of the Carotid Body: Clinical and Pathologic Considerations of 20 Tumors Affecting 19 Patients (1 Bilateral), Ann. Surg. **114**:820, 1941.

6. Winship, T.; Klopp, C. T., and Jenkins, W. H.: Glomus-Jugularis Tumors, Cancer **1**:441, 1948. Lattes, R., and Waltner, J. G.: Nonchromaffin Paraganglioma of the Middle Ear (Carotid-Body-Like Tumor; Glomus-Jugulare Tumor), Cancer **2**:447, 1949. White, E. G.: Die Struktur des Glomus caroticum und seine Beziehung zum Nervensystem, Beitr. Path. Anat. **96**:177, 1935.

7. Lattes, R.: Nonchromaffin Paraganglioma of Ganglion Nodosum: Carotid-Body and Aortic-Arch Bodies, Cancer **3**:667, 1950. Bloom, F.: Structure and Histogenesis of Tumors of the Aortic Bodies in Dogs with Consideration of Morphology of Aortic and Carotid Bodies, Arch. Path. **36**:1, 1943.

8. Wadstein, T.: Two Cases of Ganglia in the Sheath of the Peroneal Nerve, Acta orthop. scandinav. **2**:221, 1931. Foraker, A. G.: Glandlike Elements in a Peripheral Neurosarcoma, Cancer **1**:286, 1948.

9. Stout, A. P.: Ganglioneuroma of the Sympathetic Nervous System, Surg., Gynec. & Obst. **84**:101, 1947.

10. Pack, G. T.; Horning, E. D., and Ariel, I. M.: Neuroblastoma (Sympathicoblastoma), J. Neuropath. & Exper. Neurol. **11**:235, 1952.

11. Loretz, W.: Ein Fall von gangliösem Neurom (Ganglion), Virchows Arch. path. Anat. **49**:435, 1870. McFarland, J., and Sappington, S. W.: A Ganglioneuroma in the Neck of a Child, Am. J. Path. **11**:429, 1935. Bosse, M. D.; Soffel, W. A.; Nettrour, W. S., and Rohm, J. Z.: Ganglion Cell Tumors of Neck: 2 Case Reports, Am. J. Surg. **65**:120, 1944.

12. Shumacker, H. B., Jr., and Lawrence, E. A.: Cervical Sympathetic Ganglioneuroma: Case Report and Review of the Literature, Surgery **5**:572, 1939.

The clinical features are not presented. This case was similar to the one reported here in that both tumors arose from the right ganglion nodosum. In another case, reported by Clay in 1950,[1b] the tumor arose from the left nodose ganglion of the vagus nerve in a 2½-year-old girl. This tumor was successfully resected, the transection of the vagus nerve with a subsequent neurorrhaphy being necessary. The child had a persistent left vocal cord paralysis. Both the previously reported cases of ganglioneuroma of the ganglion nodosum were cases of benign tumors presenting fully differentiated, large ganglion cells. The tumor of this report differs in that it was essentially a malignant tumor containing every variant of ganglionic structure, from the large, and at times multinucleated, cells to small, anaplastic cells with large nuclei and scanty cytoplasm. Stout reports that in about 25% of all ganglioneuromas some degree of anaplasia is noted. In certain tumors the entire neoplasm will show an admixture of cells, varying from complete differentiation through all stages of undifferentiation to some which are completely anaplastic. About 18% of these tumors metastasize. In another group, one portion of the tumor will be completely differentiated, whereas another portion will present all the characteristics of a malignant neuroblastoma. Sixty-five per cent of this group produce metastases.[3a] Our patient presented the former type, with highly anaplastic cells intermingled with more differentiated ones. Malignant neuroblastomas have been known sometimes to revert to benign ganglioneuromas either spontaneously or as a result of irradiation.[13] That this occurred in our patient is highly improbable, because the radiation had been administered too recently and there were no other radiation effects noted within the tumor. This tumor must accordingly be designated as a malignant ganglioneuroma containing both benign ganglioneuromatous and malignant neuroblastomatous elements.

Clinical Features of Ganglioneuromas.—Ganglioneuromas are usually slowly growing tumors which produce no symptoms but constitute an asymptomatic mass in an accessible region. The tumors tend to compress and distort rather than infiltrate their neighboring structures. They sometimes grow to large size and in the neck may produce such symptoms as persistent cough, dyspnea, stridor, and cyanosis due to pressure against the trachea. Pressure against the laryngeal nerve may alter the quality of the voice. Pressure against sympathetic structures may produce a complete Horner syndrome or only ptosis of the eyelid. Direct vagal pressure by the tumor, as a rule, does not produce any specific symptoms. None of these symptoms occurred in our patient. Shumacker and Lawrence,[12] after reviewing the literature of cervical ganglioneuromas, summarize the significant clinical characteristics of these tumors and describe them as consisting of a slowly growing, asymptomatic mass beginning early in childhood, fixed to deeper structures, the overlying skin riding freely over the tumor, with repositioning of the carotid artery to a superficial site. These authors state that wherever the position of the carotid artery is recorded, it is described as superficially placed. The patient herein reported on manifested this symptom complex.

The diagnosis of a ganglioneuroma of the cervical region is seldom made preoperatively. A diagnosis of neuroblastoma was made in this case by an aspiration

13. Ewing, J.: Neoplastic Diseases: A Treatise on Tumors, Ed. 4, Philadelphia, W. B. Saunders Company, 1942.

biopsy and justified the plan for operative removal. It is of interest that the roentgenogram of the cervical region revealed calcific mottling within the tumor mass, a roentgenographic characteristic of neuroblastoma.[10] It would be impossible preoperatively to determine the origin of the tumor, whether from the symapthetic ganglia or the vagal ganglion nodosum. It is necessary to establish the point of origin at the time of operation, because if the tumor arises from the cervical sympathetic ganglia, the entire sympathetic chain can be severed with impunity. However, if it arises from the vagal ganglion, every effort should be made to dissect the neoplasm free from the nerve of origin because of the disturbing clinical sequelae which may result after severance of the vagus nerve. Although ganglioneuromas of the thoracic region may infiltrate the vertebral column, producing the so-called dumbbell tumor, no such instance has been recorded in the case of cervical ganglioneuromas.

Relationship of the Neuroanatomy of the Vagus Nerve to Symptoms Produced by Tumors of the Vagus.—To insure an understanding of the origin of ganglioneuromas of the ganglion nodosum of the vagus nerve and an appreciation of the clinical sequelae which result from severance of the vagus nerve during resection of the ganglion nodosum, a brief description of the neuroanatomy of this structure will be presented.

Embryonically, the vagus nerve, which is composite, takes its origin from the nucleus ambiguus of the myelencephalon and from the dorsal motor nucleus. It has several ganglia, which arise as local enlargements along the course of the ganglion crest. Certain of these are root ganglia, which include the jugular ganglion and accessory ganglia. A trunk ganglion—the nodose ganglion—is said to be a derivative of the ganglion crest, the cells migrating ventrally at a very early embryonic stage. In aquatic vertebrates the branchial arches are innervated by the vagus nerves.[14] It is thus understandable that the derivatives of the fourth and fifth pairs of branchial arches in mammals—the muscles of the pharynx and larynx—are innervated by the vagus. This nerve also supplies the smooth muscles of the viscera.

Figure 1 demonstrates the anatomy of the vagus nerve and shows the ganglionic and paraganglionic structures of the parasympathetic system which give rise to the tumor under discussion. A point of considerable interest is the origin of the recurrent laryngeal nerve from the vagus. It will be noted that on the right side the recurrent laryngeal nerve branches from the vagus inferior to the right subclavian artery, whereas on the left side the recurrent nerve arises deep within the thorax. It is thus possible to sever the right vagus nerve inferior to the site where the recurrent nerve branches, in which case the laryngeal symptoms associated with paralysis of the recurrent nerve will not develop. This would not be possible on the left side. The severance of either vagus at the level of the nodose ganglion would produce all the pharyngeal and laryngeal symptoms associated with vagal severance. These would include (1) motor disturbances (aphonia; dysphonia; dysphagia associated with regurgitation, esophagospasm, cardiospasm, or pylorospasm, and paralysis of the soft palate with loss of gag reflex); (2) sensory dis-

14. Arey, L. B.: Developmental Anatomy: A Textbook and Laboratory Manual of Embryology, Ed. 2, Philadelphia, W. B. Saunders Company, 1930.

turbances (pain or paresthesia of the pharynx or larynx, or anesthesia of these structures in complete lesions; a constant cough due to vagal irritation, and certain respiratory disorders, such as dyspnea and pseudoasthma, arising from interruption of vagal control of respiration, and hyposecretion of saliva in some instances), and (3) parasympathetic disturbances, which might include tachycardia and dilatation of the stomach.[15] Many of these symptoms occurred to a rather marked degree in our patient during the immediate postoperative period and were due undoubtedly to unavoidable trauma to the nerve structures during resection of the tumor. The fact that all symptoms completely subsided within four months after operation demonstrates that tumors of the nodose ganglion can be safely resected without permanent damage to the nerve. The patient presented no cardiac arrhythmias or intra-abdominal symptoms. Tachycardia, which she manifested postoperatively, could be the result of vagal disturbance, or it might represent a reaction to infection or other surgical complications. (Postoperatively the electrocardiogram was normal except for sinus tachycardia. The auricular and ventricular rates were 171 beats per minute.) Clay mentions resection of this segment of the vagus nerve in seven instances reported in the literature. In only one of the cases was there any cardiorespiratory or gastrointestinal disturbance. He states that postoperative vocal paralysis was a constant finding in each of these patients, as it was in his own patient.[1b]

Treatment of Ganglioneuromas of the Neck.—The treatment should always be complete surgical extirpation. Because these tumors grow relentlessly and compress contiguous structures, they should be removed as soon as the diagnosis is suspected. Since ganglioneuromas do not infiltrate adjacent structures, they can usually be dissected free of the tumor bed completely and with ease. Their point of attachment is a location where great care must be exercised in resecting the tumor. Laryngeal paralysis was avoided by dissecting the tumor free from the vagus nerve in our patient. If it is not possible to dissect the tumor free of the nerve, then it will become necessary to transect the nerve and attempt a primary neurorrhaphy, being certain to maintain proper alignment of the nerve edges during the repair. Ganglioneuromas arising from ganglia of the sympathetic nervous system may have the sympathetic nerve elements resected with the neoplasm. The only unwelcome complication of this procedure is the development of a Horner syndrome. It is of interest that although our patient had a malignant ganglioneuroma, the tumor was grossly smooth, apparently encapsulated, and discrete, although adherent to contiguous structures of importance. The tumor should always be completely extirpated, and the practice of certain surgeons of partially resecting ganglioneuromas [16] is not to be condoned, because 18% of all ganglioneuromas present histologic evidence of anaplasia.[3a]

Irradiation does not appear to be indicated for treating malignant ganglioneuromas, and it should never be used as a substitute for surgical excision of an operable neoplasm. Although the neuroblastomatous elements should be sensitive, as are adrenal neuroblastomas, the ganglionic elements are notoriously radiore-

15. McDonald, J. J.; Green, J. R., and Lange, J.: Correlative Neuroanatomy, Ed. 3, Chicago, University Medical Publishers, 1942.

16. Godwin, J. T.; Watson, W. L.; Pool, J. L.; Cahan, W. G., and Nardiello, V. A., Jr.: Primary Intrathoracic Neurogenic Tumors, J. Thoracic Surg. **20**:169, 1950.

sistant. The ganglioneuroma of this report did not manifest any evidence of x-ray effect, either clinically or histologically, after a significant dose of high-voltage x-rays.

End-Results in Ganglioneuroma.—Nothing can be said concerning the prognosis in this case because the patient was treated too recently. Of the two other patients with ganglioneuroma of the vagal nodose ganglion, one was dead at the time of the report. The nature of the death and whether or not it was due to the ganglioneuroma was not recorded, as only the pathologic features of the tumor were presented. The other patient was alive and apparently free from disease four and a half years after resection.[17] It is hoped that a propitious prognosis will be enjoyed by our patient. No metastases were observed in the neck at the time of the resection, and there is no discernible evidence of distant metastases. The patient is apparently free from neoplastic disease at present.

17. Clay, R.: Personal communication to the authors.

WOUND HEALING WITHOUT DRESSINGS

Clinical Study

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ST. LOUIS

THE APPLICATION of dressings to surgical wounds is a custom as old as recorded history. The chief reasons for applying dressings are for absorbing secretions, aiding hemostasis, splinting, obliterating dead spaces, protecting against trauma, and preventing contamination. Before aseptic surgery, perhaps the principle reason was to absorb secretions; with the advent of aseptic surgery, the main consideration was prevention of bacterial contamination. The present study was not an attempt to question the validity of using dressings or to impugn the above fundamental precepts. Instead, our purpose was to determine whether the application of a dressing per se had any significant effect on wound healing.

An attempt was made to evaluate this problem experimentally.[1] We produced clean aseptic incised wounds of the abdominal walls of rabbits, obtained hemostasis, and carefully coaptated the edges, covering the wounds of half of the animals with dressings and leaving the others uncovered. Gross and microscopic sections of these wounds were obtained on representative postoperative days. It was shown that wounds healed equally well, whether covered or not covered by dressings. As a corollary, it was also shown that an uncovered wound is rapidly sealed by a coagulum of red blood cells and fibrin and that this early seal gives considerable tensile strength to the wound and prevents bacterial contamination. It is realized that accurate controls in such experiments can only be approached, for the application of the simplest dressing also exerts hemostasis, splinting, and antitraumatic effects not existent when the wound is left uncovered. However, the benefits would favor the group with dressings.

Well-controlled clinical experiments comparing the healing of wounds in human beings with and without dressings are even more difficult to achieve. There have been sporadic efforts to leave selected wounds without dressings. Hippocrates

From the Surgical Division of Homer G. Phillips Hospital, the Department of Surgery of the Jewish Hospital, and the Department of Surgery, Washington University School of Medicine.

1. Heifetz, C. J.; Lawrence, M. S., and Richards, F. O.: Comparison of Wound Healing With and Without Dressings: Experimental Study, A. M. A. Arch. Surg. **65**:746-751 (Nov.) 1952.

thought that wounds of the head should be left unbandaged.[2] Many surgeons habitually leave clean surgical wounds of the face and other parts of the body uncovered. Berkeley and Bonney [3] wrote, in 1943, that 27 years earlier they had given up all dressings for clean gynecologic abdominal wounds, covering the closed wound in the operating room only with a sterile towel. Mengert and Hermes [4] have not been covering abdominal wounds created for gynecological operations since 1946. They found in 100 consecutive patients, half of each wound being covered and the other half being uncovered by dressings, no appreciable differences in wound complications between the dressed and undressed portions of the wounds. Bacterial colonies taken from the two halves of the wound were also stated to be numerically equal, although pathogenic organisms were more numerous under the dressings. The exact methods used in their bacteriological studies were not described. Sister Mary John,[5] in a survey made to determine how much gauze is needed to protect adequately clean wounds, found that some surgeons had empirically adopted the principle of leaving certain wounds uncovered. She quoted Hauman as stating that he had compared a series of uncovered surgical wounds with a series dressed with thin gauze and found no increase in the incidence of wound infection in the undressed surgical wounds. For the most part, clinical impressions form the basis for leaving dressings off clean operative wounds.

CLINICAL STUDIES

Homer G. Phillips Hospital.—To compare dressed wounds with wounds uncovered by dressings in human subjects, we studied 53 undrained aseptic surgical wounds on 48 patients at the Homer G. Phillips Hospital. The patients ranged in age from 10 to 90 years. Thirty-nine were male, and nine were female. There were 30 inguinal hernioplasties, 15 appendectomies, 1 cholecystectomy, 2 thyroidectomies, 4 exploratory laparotomies, and 1 umbilical hernioplasty. Wounds exposed to bacterial contamination were excluded from our study. The operations were performed by four members of the resident house staff at the fourth- and fifth-year levels. Fundamentals leading to good wound healing were rigidly observed by these operators. They included careful cleansing of the operative site, single-stroke incisions through the skin and subcutaneous tissue where possible, gentle handling of tissues, avoidance of unnecessary tissue clamping, careful hemostasis, use of fine silk, and careful coaptation of the tissue layers with nonstrangulative interrupted sutures. Local anesthesia was not used.

The 53 wounds were divided into three groups:

Group I contained 18 wounds which were covered at the termination of the operations by the customary small gauze dressings, sometimes reinforced with abdominal pads, and secured with adhesive tape.

Group II contained 16 wounds covered by similar dressings, which were removed 24 hours later. This management was evaluated, because it seemed to combine some of the needs for placing a dressing on a wound with the advantages of leaving one off.

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2. Peterson, W. F.: Hippocratic Wisdom for Him Who Wishes to Pursue Properly the Science of Medicine: A Modern Appreciation of Ancient Scientific Achievement, Springfield, Ill., Charles C Thomas, Publisher, 1946, p. 103.

3. Berkeley, C., and Bonney, V.: Textbook of Gynecological Surgery, Ed. 4, New York, Paul B. Hoeber, Inc., 1943, p. 25.

4. Mengert, W. F., and Hermes, R. L.: Simplified Gynecological Care, Am. J. Obst. & Gynec. **58**:1109-1116 (Dec.) 1949.

5. Mary John, Sister: How Many Sterile Gauze Sponges are Needed Adequately to Protect a Clean Wound? Read before the American Association for Advancement of Science, St. Louis, Dec. 27-30, 1952.

Group III contained 19 wounds which were left without dressings at the termination of the operations, except for leaving a sterile towel on for 6 to 24 hours.

Bacterial Counts: The following technique for obtaining bacterial counts was employed. Plain transparent water-permeable Cellophane (donated by Brooks Paper Company, St. Louis),

TABLE 1.—*Bacterial Colonies Obtained from Skin* *

Wound	Patient †	Operation	No. of Colonies: 1st Post-operative Day	2nd Post-operative Day	4th Post-operative Day
		Group I—Dressing			
1	E. R.	Hernioplasty	236	206	208
2	A. B.	Hernioplasty	800	740	652
3	J. S.	Appendectomy	460	224	186
4	J. D.	Appendectomy	470	620	480
5	S. W.	Appendectomy	400	610	250
6	M. H.	Hernioplasty	467	520	210
7	M. M.	Hernioplasty	400	230	180
8	L. B.	Appendectomy	396	471	250
9	H. S.	Hernioplasty	523	423	400
10	J. S.	Appendectomy	161	22	109
11	G. K.	Appendectomy	286	169	408
12	B. V.	Hernioplasty	14	6	204
13	L. W.	Appendectomy	480	500	410
14	L. C. (*A*)	Hernioplasty	620	640	280
15	A. W.	Explor. laparotomy	230	492	322
16	J. A.	Explor. laparotomy	69	140	184
17	J. J.	Thyroidectomy	618	810	420
18	L. M. (*B*)	Hernioplasty	438	600	864
		Mean	393	431	330
		Group II—Dressing 24 Hr.			
19	S. B.	Hernioplasty	700	300	100
20	J. W.	Appendectomy	400	36	12
21	A. T.	Appendectomy	298	48	300
22	C. M.	Appendectomy	130	32	6
23	C. H.	Appendectomy	8	16	6
24	H. B.	Appendectomy	96	470	432
25	M. B. (*C*)	Bilateral hernioplasty	27	30	28
26	J. D.	Bilateral hernioplasty	731	21	28
27	S. L.	Appendectomy	180	88	100
28	M. L.	Hernioplasty	203	93	541
29	F. K.	Hernioplasty	960	267	980
30	F. M.	Explor. laparotomy	24	206	85
31	J. S.	Hernioplasty	18	32	24
32	L. P.	Hernioplasty	630	782	420
33	L. M. (*B*)	Bilateral hernioplasty	492	456	240
34	D. W.	Appendectomy	428	401	400
		Mean	333	206	231
		Group III—No Dressing			
35	H. R.	Hernioplasty	233	632	120
36	L. C. (*A*)	Hernioplasty (inguinal)	48	69	52
37	L. C. (*A*)	Hernioplasty (umbilical)	120	38	40
38	C. S.	Hernioplasty	840	640	600
39	R. M.	Hernioplasty	960	900	980
40	A. C.	Hernioplasty	549	1,004	599
41	C. H.	Hernioplasty	610	10	577
42	M. S.	Cholecystectomy	527	618	496
43	M. S.	Thyroidectomy	516	483	429
44	T. D. (*D*)	Bilateral hernioplasty	35	20	18
45	T. D. (*D*)		36	30	16
46	J. A.	Hernioplasty	700	600	400
47	C. H.	Appendectomy	8	284	106
48	V. C.	Explor. laparotomy	377	91	280
49	J. Y.	Hernioplasty	602	200	250
50	E. M.	Hernioplasty	640	540	320
51	M. B. (*C*)	Hernioplasty	106	10	52
52	W. N.	Hernioplasty	102	104	86
53	J. P.	Hernioplasty	32	106	98
		Mean	271	288	290

* Areas of skin were 4 sq. in. (25 sq. cm.).
† Four patients, *A*, *B*, *C*, and *D*, had more than one wound (Table 3).

300 weight, was cut into squares exactly 2 by 2 in. (5 by 5 cm.) and were kept sterile in a bath of 70% alcohol. (Heat sterilization caused Cellophane to curl up or wrinkle, so that it could not be used for our purpose.) Just before using, the operator put on a mask and sterile gloves. Handling the Cellophane square with sterile instruments, it was washed with sterile

water and dried on a sterile towel. The square was then compressed for two seconds to the center of the wound and placed, contaminated side up, on a sterile blood-agar plate. After the bacterial imprint was made, the wounds of Group I were covered by sterile dressings. The agar

TABLE 2.—*Bacterial Colonies Obtained from Skin* *

Wound	Patient	No. of Colonies		
		1st Postoperative Day	2nd Postoperative Day	4th Postoperative Day
	Hernioplasty			
1	E. R.	236	206	208
2	A. B.	800	740	653
6	M. H.	467	520	210
7	M. M.	400	230	180
9	H. S.	523	423	400
12	B. V.	14	6	204
14	L. C.	620	640	280
18	L. M.	438	600	864
19	S. B.	700	300	100
25	M. B.	27	30	28
26	J. D.	731	21	284
28	M. L.	203	93	541
29	F. K.	960	267	980
31	J. S.	18	32	24
32	L. P.	630	782	420
33	L. M.	492	456	240
35	H. R.	233	632	120
36	L. C.	48	69	52
38	C. S.	840	640	600
39	R. M.	960	900	980
40	A. C.	549	1,004	599
41	C. H.	610	10	577
44	T. D.	35	20	18
45	T. D.	36	30	16
46	J. A.	700	600	400
49	J. Y.	602	200	250
50	E. M.	640	540	320
51	M. B.	106	10	52
52	W. N.	102	104	86
53	J. P.	32	106	98
	Mean	425	340	318
	Appendectomy			
3	J. S.	460	224	186
4	J. D.	470	620	480
5	S. W.	400	610	250
8	L. B.	396	471	250
10	J. S.	161	22	109
11	G. K.	286	169	408
13	L. W.	480	500	410
20	J. W.	400	36	12
21	A. T.	298	48	300
22	C. M.	130	32	6
23	C. H.	8	16	6
24	H. B.	96	470	432
27	S. L.	180	88	100
34	D. W.	428	401	400
47	C. H.	8	284	106
	Mean	280	266	230
	Other Operations †			
15	A. W.	230	492	322
16	J. A.	69	140	184
30	F. M.	24	206	85
37	L. C.	120	38	40
42	M. S.	527	618	496
48	V. C.	377	91	280
17	J. J.	618	810	420
43	M. S.	516	483	429
	Mean	310	362	293

* Areas of skin were 4 sq. in. (25 sq. cm.).
† Laparotomy, wounds 15, 16, 30, 37, 42, and 48; thyroidectomy, wounds 17 and 43.

plates were incubated for 24 hours, and the count of bacterial colonies was obtained. Bacterial counts were obtained from all of the 53 wounds on the first, second, and fourth postoperative days. No attempt was made to identify the type of micro-organisms. The bacterial counts are shown in Table 1. Both low and high counts were obtained in all three groups; the variations

were between 6 and 1,004. A low or high bacterial count on the first day usually remained in a low or in a high range, respectively, on the second and fourth days.

The bacterial counts grouped according to type of operation are shown in Table 2. Table 3 contains the bacterial counts obtained from the nine wounds of the four patients with multiple operations.

An analysis [6] of variance was performed between bacterial counts obtained from wounds with dressings (Group I), wounds dressed for 24 hours (Group II), and wounds without dressings (Group III), and bacterial counts were obtained on the first, second, and fourth postoperative days. No significant differences existed between dressings or postoperative days, or was there significant interaction between these variables. In other words, those differences which existed could be attributed to chance fluctuations.

An analysis of variance was performed between bacterial counts obtained from the three operative groups (Table 2). No significant differences existed between bacterial counts found following the various types of operations.

Wound Healing: The wounds were examined on the third, fifth and seventh postoperative days, and notations of any wound complications were made. All 53 wounds healed by primary union and without major infection. The wounds of three patients of Group I (with dressings)

TABLE 3.—*Bacterial Colonies Obtained from Skin of Patients with Multiple Wounds*

	Patient	Operation	Group	1st Postoperative Day	2nd Postoperative Day	4th Postoperative Day
A	L. C.	Inguinal hernioplasty, rt.	Covered (I)	620	640	280
		Inguinal hernioplasty, lt.	Uncovered (III)	48	69	52
		Umbilical hernioplasty	Uncovered (III)	120	38	40
B	L. M.	Inguinal hernioplasty, rt.	Covered 24 hr. (II)	492	456	240
		Inguinal hernioplasty, lt.	Uncovered (III)	438	600	864
C	M. B.	Inguinal hernioplasty, rt.	Covered 24 hr. (II)	27	30	28
		Inguinal hernioplasty, lt.	Uncovered (III)	106	10	52
D	T. D.	Inguinal hernioplasty, rt.	Uncovered (III)	35	20	18
		Inguinal hernioplasty, lt.	Uncovered (III)	36	30	16

* Areas of skin were 4 sq. in. (25 sq. cm.).

and of one patient of Group III (no dressing) appeared somewhat edematous. Still another wound of a patient of Group I presented two small stitch abscesses. These minor complications are not statistically significant.

Psychic Reactions: Controlled psychological studies of our patients were not performed. However, we did attempt to obtain impressions of psychic reactions by recording actual expressions of the patients whose wounds were left uncovered. These impressions were that the patients of Groups II (dressings for 24 hours) and III (no dressings) made at least as satisfactory adjustments to the postoperative state and to hospital routine as those patients of Group I (dressings). Actually we thought that some of Group II and Group III may have been more adaptable and cooperative because they enjoyed participating in our clinical study.

Eight of the 19 patients of Group III (no dressings) were informed in advance of the operation that they would find their wounds exposed after the operation. The other 11 patients did not find this out until after the operation. Comparing the two subgroups, we were of the opinion that there were no appreciable differences in their postoperative reactions.

Seven of the 16 patients of Group II (dressings for 24 hours) were informed in advance of the operation that their dressings would be removed after 24 hours. The other nine patients (one also belonged to Group III) were not told that their dressings would be removed in 24 hours. These two subgroups also had similar postoperative reactions.

6. Statistical data were computed by members of the Department of Psychology, Washington University.

Of the 15 patients of Groups II and III who were informed of our plan before surgery, 9 expressed preoperative fear that untoward results such as infection, disruption, or injury might occur if the wounds were left uncovered. All nine of these patients completely overcame these fears by the second postoperative day.

Most of the 32 patients whose wounds were left without dressings sooner or later expressed satisfaction in seeing the progress of their wounds from day to day. One patient with a history of another operation was favorably impressed, because adhesive tape did not have to be removed. Three patients with bilateral inguinal hernioplasties, one side covered and the other side uncovered, gave the opportunity to compare their reactions to the two types of treatment. The following are some interesting comments: "I like to look at it; the side without the dressing feels better." "Is something wrong with the covered side? Why not take it off?" The patient with three wounds, two uncovered and one covered, said, "They all hurt, and I don't know which is worse. The open one looks good; wonder how the one with the bandage is doing." One patient favored the side with a dressing: "The side that is covered feels better than the other." A day later, however, he said, "They are both fine."

Morbidity: The average duration of stay in the hospital following these operations was almost identical in the three groups of patients. In some instances we were tempted to send home earlier those patients whose wounds had no dressings, since we knew earlier that they were getting along well. However, they were left in the hospital until after their sutures were removed, generally on the seventh postoperative day.

Jewish Hospital.—Concomitantly with the rabbit experiments [1] and those described above, one of us (Heifetz) has been making observations on his private general surgical patients at the Jewish Hospital. Selecting the wounds to be left without dressings according to the rigid restrictions to be discussed below, 102 patients with 108 wounds have left the operating room with the wound covered only by a towel. This included 63 inguinal hernioplasties, 3 umbilical hernioplasties, 30 appendectomies, 3 thyroidectomies, and 9 other laparotomies. It represented almost one-fourth of the operations he has done during this time at the Jewish Hospital. Excluded from these figures are herniotomies of infancy and childhood. These wounds are painted with collodion and left uncovered.[7] In other patients, 28 dressings were removed on the first, 9 on the second, and 3 on the third postoperative days.

A comparison between these patients and those who had customary dressings cannot be made. The last group, containing drainage cases and intestinal operations, were the most serious operations, and wound complications were to be expected.

The wounds without dressings and those with dressings which were removed early all healed without major infection. A few stitch abscesses occurred. A few uncovered wounds also showed some redness and edema of the edges, but there was no interference with wound healing. Even though more experience has been gained with this method of handling wounds, the percentage of wounds left uncovered has not increased; the criteria have not been relaxed.

The assurance gained from observing exposed wounds has made it possible to send some patients home earlier after their operations than patients with concealed wounds. Recently, some herniotomy and appendectomy patients have left the hospital as early as the fourth postoperative day. This has lowered patients' hospital costs, used less of the surgeon's time for rounds, and made beds available in a hospital sorely taxed to meet bed requirements.

COMMENT

The results of these observations seem to corroborate our conclusions from experiments on rabbits [1] that the application of a dressing to a clean undrained well-coaptated wound has no significant gross effect on wound healing. Our experiments also prove that bacterial counts taken from aseptic wounds on representative postoperative days show statistically no significant differences, whether or not the wounds were dressed. A close examination of the data suggests that bacterial counts were

7. Heifetz, C. J.: Surgery for Inguinal Hernias in Infancy and Childhood, Am. J. Surg. **83**:653-663 (May) 1952.

lower oftener when the wounds were left without dressings, but the statistical analyses show that this tendency could be explained on the basis of chance variation. A repetition of these experiments with more rigid controls may reveal whether uncovered wounds actually show less bacterial contamination. We plan to identify the organisms and to make studies of sweating and temperatures on dressed and undressed wounds.

Certainly there is nothing in our experiments to show that placing a dressing on a clean surgical wound makes a more favorable bacterial environment for wound healing. The concept, widely held since the beginning of the aseptic era of surgery, that dressings aid in preventing bacterial infection may accordingly require alteration. We are anxious to point out, however, that those bacteria present stand a greater chance of initiating infection in wounds where hemostasis is not controlled and where dead spaces have been left. If these contributors to infection cannot be controlled, or if splinting must be secured, or if trauma must be precluded, by all means a dressing should be applied. If these factors, however, have been controlled, we see no need for a dressing.

Since dressings are not needed on many clean well-coaptated surgical wounds, there are advantages to leaving them off. The wounds can be more frequently observed by the surgeon, the house staff, and the nurse. Adhesive tape irritation is avoided. Economies in surgical supplies and in time and effort of hospital personnel are made possible, a fact which should appeal to surgeons, nurses, and hospital administrators. The possibility of reducing hospital stay in some cases is likewise appealing, especially to the patient.

At the Homer G. Phillips Hospital the average patient of the type included in our study formerly required two dressings, one placed on the wound in the operating room, the other during the usual dressing change for suture removal, each costing about $0.40. On the general surgical service at least 50 patients are operated on each month, whose dressings could well be omitted. This would save the hospital $40.00 a month or $480.00 a year. Homer G. Phillips Hospital contains 700 of the 640,207 general hospital beds in the United States.[8] If a similar ratio of general surgical beds and types of operations were maintained throughout the country, a potential saving of $438,984.00 from dressings alone is possible.

We have also found that each patient's second dressing required 10 minutes of the floor nurse's time. There being 50 such dressings a month, a minimum of 100 hours a year are required for this service. At prevailing graduate nurses' pay of about $1.50 per hour, one can compute a saving of $150.00 a year. For the country at large this saving could be $137,182.00.

These figures do not take into consideration the considerable cost of instruments used in dressings and their sterilization, the use of personnel to set up dressing carts, and the time expended by the house staff. They omit the cost of extra dressings performed on some patients. Moreover, the figures represent savings only in general surgery and leave out potential savings in other surgical services, notably gynecology. They do not take into consideration the great amount of surgical work done in special types of hospitals. If these additional costs could be computed, savings many times the above figures would be represented.

8. Arestad, F. H., and McGovern, M. A.: Hospital Service in the United States, J. A. M. A. **149**:149-167 (May) 1952.

RECOMMENDATIONS

On the basis of these experiments and clinical observations, the following criteria have been set down for deciding which wounds require dressings and which wounds may be left uncovered.

Dressings Required.—The following are wounds which require dressings: (1) those of operations done with local infiltration anesthesia (false assurance of hemostasis created by the epinephrine used with the anesthetic agent); (2) drainage wounds and contaminated wounds which may cause infection; (3) wounds through scars of previous operations; (4) wounds in which bleeding has not been completely controlled, including a small percentage of wounds which continue to ooze in spite of clamping and tying of bleeders; (5) wounds in which tissues have been roughly handled; (6) wounds closed with catgut; (7) wounds closed hastily because of the nature of the operation or the condition of the patient; (8) wounds with potential or actual dead spaces; (9) wounds requiring splinting; (10) wounds subject to trauma because of location or because of an uncooperative patient.

Any one of the above conditions makes necessary the application of a dressing. Once one has been applied, the surgeon should soon give thought to removing it. Since the requirements of hemostasis, obliteration of dead space, and splinting are frequently satisfied after 24 hours, it is often possible to remove the dressings at that time, but we have seen fit to leave some on for 48 or 72 hours, and some are left on until the sutures are removed.

No Dressings Required.—The following are the requirements for leaving dressing off: (1) no local anesthesia, (2) sharp dissection and minimal undermining of tissue planes, (3) gentle handling of tissues, (4) careful clamping and tying of all bleeders, (5) dead spaces eliminated, (6) nonabsorbable fine sutures, (7) careful layer coaptation without strangulation of tissues, (8) absence of contamination (e. g., by intestinal contents), (9) no drains.

All these requirements should be met before deciding to leave the dressing off. When dressings are not applied, we express the accumulated blood and air, check the skin approximation, and cover the wound with a towel held to the skin with a strip of adhesive tape. The towel is for protection against trauma while moving the patient and during recovery from anesthesia; it is generally removed in a few hours.

Inguinal hernia wounds lend themselves particularly well to this practice, especially if the incision is made transversely along the skin lines. Other wounds which we have left uncovered include appendectomies, umbilical hernias, cholecystectomies (without drainage), exploratory laparotomies, gynecological operations, and thyroidectomies. Since this work was performed by general surgeons, the possibility of including other types of operations was not explored. Abdominal gynecological operations would seem to be ideal for this type of management.

Indications for the use of antibiotics should rest on factors other than whether or not a dressing is used. In general, when dressings are not used, wound conditions are such that antibiotics are not required.

Patients cooperate well in nearly all instances when their wounds are not covered by dressings, and their acceptance of this procedure is similar whether or not they are forewarned.

CONCLUSIONS

Fifty-three aseptic undrained well-coaptated surgical wounds in human subjects were divided into three groups. The wounds of the patients of Group I were covered in the operating room by customary dressings, which were left on until the sutures were removed. The wounds of the patients of Group II received similar dressings, but they were removed in one day. The wounds of the patients of Group III were covered only by a sterile towel, which was removed in 6 to 24 hours.

Bacterial counts obtained from the wounds on the first, second, and fourth postoperative days showed considerable variation. Statistical computation of these counts showed no significant differences in the three groups in the three postoperative days, in the categories of operations, or in the interaction between these variables.

Equal and satisfactory wound healing occurred in all three groups.

There was ready acceptance by patients of the principle of leaving wounds without dressings.

Satisfactory healing has also been obtained in 108 other wounds without dressings. These operations included hernioplasties, appendectomies, thyroidectomies, cholecystectomies without drainage, and pelvic laparotomies.

Rigid criteria which must be fulfilled before a dressing is left off have been enumerated. These include avoidance of local anesthesia, careful handling and clamping of tissues, elimination of dead spaces, complete control of bleeding, use of fine nonabsorbable sutures, careful approximation of layers, and absence of contamination and drainage.

Those wounds which always require the application of a dressing are described. It is possible to remove dressings from some of these wounds in 24 hours.

The advantages of leaving dressings off include the opportunity to observe the wounds more often, avoidance of irritation from adhesive tape, economies in surgical supplies and in time and effort of hospital personnel and surgeons, and occasionally reduction in hospital stay.

A wide acceptance of the principle of leaving dressings off carefully selected wounds will save hospitals a considerable sum of money.

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SURGICAL CLOSURE OF ATRIAL SEPTAL DEFECTS

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DURING the last decade and a half, impressive strides have been made in surgery in the development of procedures for the cure or alleviation of various congenital abnormalities of the heart and great vessels. Within the past year it has become evident that defects of the interauricular septum should be added to the list of anomalies for which surgical attack now has much to offer. In several centers throughout the country methods have been devised, employing different techniques, whereby in human beings it is possible with a reasonable degree of safety to approach the atrial septum and to close apertures which are found therein. The technical aspects of these surgical undertakings have been recorded in detail by Bailey and his associates,[1] Gross and his colleagues,[2] Lewis and Taufic,[3] Swan,[4] and others. The present communication is a summary of observations on a group of patients who have been subjected to operative attempts for closure of interauricular septal openings, giving particular attention to the evaluation of the surgical efforts and also to the development of policies regarding the selection of patients who might be benefited by such procedures.

SURGICAL CONSIDERATIONS

The methods currently available for surgical closure of atrial defects include the following: 1. It is possible to employ a pump-oxygenator apparatus to take over temporarily the functions of the patient's lungs and heart so that the latter can be widely opened and the defect repaired. Gibbon [5] has recently been successful in

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1. Bailey, C. P.; Downing, G. D.; Geckeler, G. D.; Likoff, W.; Goldberg, H.; Scott, J. C.; Janton, O., and Redondo-Ramirez, H. P.: Congenital Interatrial Communications: Clinical and Surgical Considerations with a Description of a New Surgical Technique: Atrio-Septo-Pexy, Ann. Int. Med. **37**:888, 1952.

2. Gross, R. E.; Watkins, E., Jr.; Pomeranz, A. A., and Goldsmith, E. I.: A Method for Surgical Closure of Interauricular Septal Defects, Surg., Gynec. & Obst. **96**:1, 1953.

3. Lewis, F. J., and Taufic, M.: Closure of Atrial Septal Defects with the Aid of Hypothermias: Experimental Accomplishments and the Report of One Successful Case, Surgery **33**:52, 1953.

4. Swan, H.: Surgical Closure of Interauricular Septal Defects, J. A. M. A. **151**:792, 1953.

5. Gibbon, J.: Personal communication to the authors.

achieving a brilliant result in this manner. The complexities of the technique are great, and although the use of such a machine should be enormously helpful in the repair of interventricular defects, it would appear at present to be rather cumbersome and unnecessary for the treatment of most atrial lesions which we now know can be cured by simpler methods. 2. By a combination of refrigeration of the patient and temporary clamping of the venae cavae, the heart can be opened for periods of

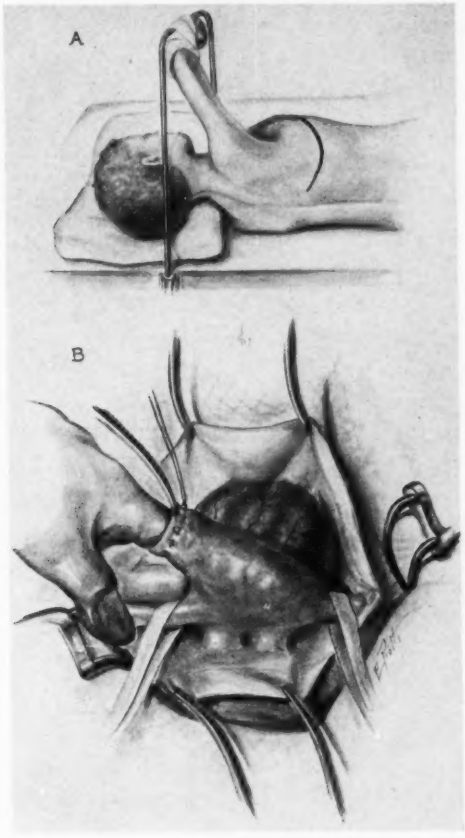

Fig. 1.—Method for closure of interauricular septal defect, applicable when the opening lies posteriorly and is not excessively large. *A*, position of patient; approach through the fifth interspace. *B*, pericardium opened, exposing the right side of the heart. After purse-string is placed around the tip of the right auricular appendage, this structure is opened and an exploring finger is passed into the atrium. (If digital exploration shows a posterior midlevel septal opening, we proceed with a repair as shown in Figures 2 and 3; if the defect is found elsewhere in the septum, we prefer to withdraw the finger, close the appendage, and proceed with a "well" operation, indicated in Figure 4).

eight or nine minutes for manipulations within its interior. The operating time can be lengthened by using two (or more) periods during which the circulation is stopped, permitting a resumption of flow between the intervals. Successes have been reported by Lewis and Taufic,[3] Swan,[4] and others. While this method seems applica-

ble to the young and hearty, it is apparently much more risky for older persons. Furthermore, there is likely to be a feeling on the part of the surgeon of considerable pressure and anxiety to finish the operation in a short specified time—which is sufficient in the average group of cases but which can be a considerable handicap if unusual circumstances are encountered within the heart. 3. The lateral wall of the

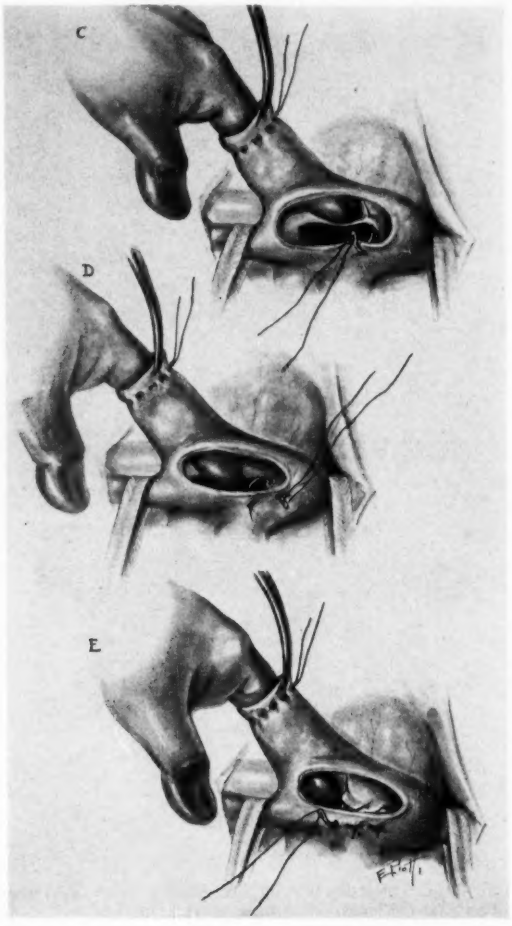

Fig. 2.—Closure of posterior septal defect. *C*, silk stitch passed through posterior wall of auricle, grasping the anterior edge of the septum, guiding the manipulation with the finger within the auricle. *D*, needle turned and stitch brought out through posterior wall of auricle, making a mattress suture. *E*, two mattress sutures have been placed, each having been snugged up and tied immediately after it was placed; each progressively closes the septal opening and facilitates placing of a subsequent stitch. Row of sutures is continued until septal opening is completely closed.

enlarged right auricle can be inverted in such a manner that it is made to plug the atrial opening by suturing it to the surrounding rim of septal tissue, as described by Bailey.[1] This has been highly effective in many cases but probably carries the dis-

advantage—or certainly the risk—of sometimes blocking the orifice of a vena cava or the tricuspid valve, if the defect happens to be located in juxtaposition to one of these areas. 4. For posterior defects, which are neither very high nor very low in the septum, it is amazingly easy to obtain closure by drawing the septal edge back to the posterior wall of the auricle with mattress sutures, as shown here in Figures 1 to

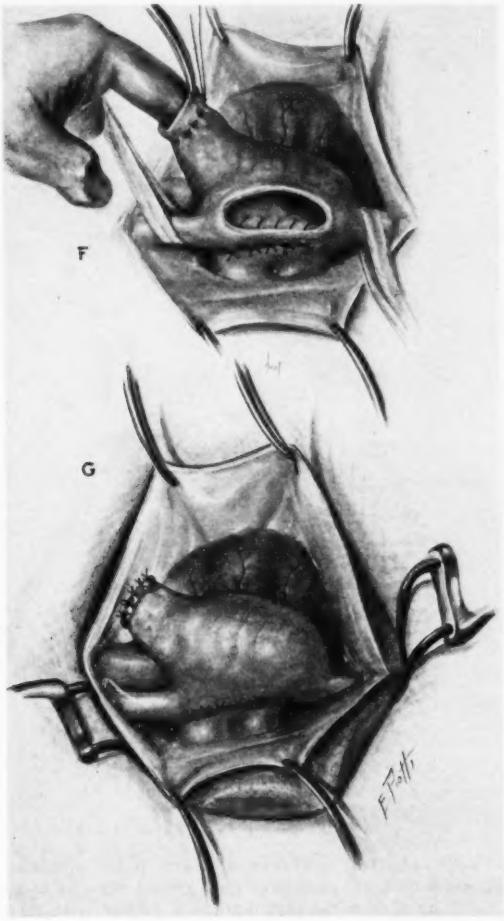

Fig. 3.—*F*, closure of the septal defect has been completed, with finger being withdrawn from the auricular appendage. *G*, tip of appendage closed with a row of figure-of-eight non-absorbable surgical (silk) sutures.

3. We have been able to perform the steps by passing a finger into an auricle (through the appendage), effectively and thoroughly closing the septal orifice, withdrawing the finger, and suturing the auricular appendage, all in less than 10 minutes. The technique is so simple, gives so little disturbance to the heart, and is so successful in repairing the lesion, that it appears without doubt the method of choice for

treatment of all defects which lie in the central posterior part of the septum. 5. For those lesions which may be very high, very low, or very far forward, and for all of the openings which are great in size, a rubber "well" can be attached to the opened auricle [2] (Fig. 4), forming a pool of blood through which the fingers can be passed into the auricular chamber, allowing by tactile direction with the fingers a repair of

Fig. 4.—Atrial "well" operation, used in cases which are not amenable to the simpler procedure shown in Figures 1 to 3. *A*, position of chest wound, same as in Figure 1*A*. *B*, attachment of a rubber "well" to wall of the right auricle. *C*, rubber well in place, the atrial wall widely open in the base of the rubber sac, giving a pool of blood through which fingers can be run to treat the septal defect, as shown in Figures 5 or 6.

the septal opening by direct suture (Fig. 6) or by the onlay of a polyethylene sheet (Fig. 7) which is made to cover the opening. This foreign material, from observations on dogs, has been found to be tolerated very well and is known to become covered over with fibrous tissue and endocardium. It has been placed in three of our patients, in whom it has remained for more than a year without any complications or untoward effects.

All of the above methods are found to have shortcomings when dealing with a very low septal defect in which there is no rim of septum to grasp near the base of the tricuspid and mitral valves.

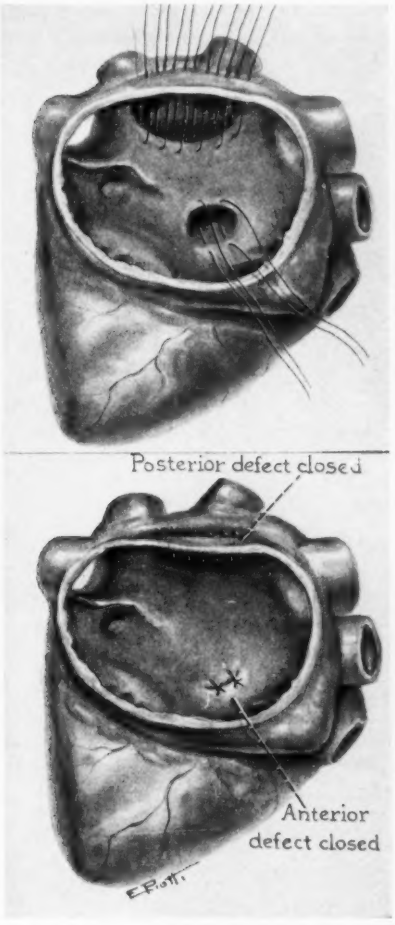

Fig. 5.—By working through a rubber "well" (omitted here for purpose of clarity) narrow openings in the septum can be closed by sutures with silk. In the case here depicted, two septal defects were found and were repaired as shown.

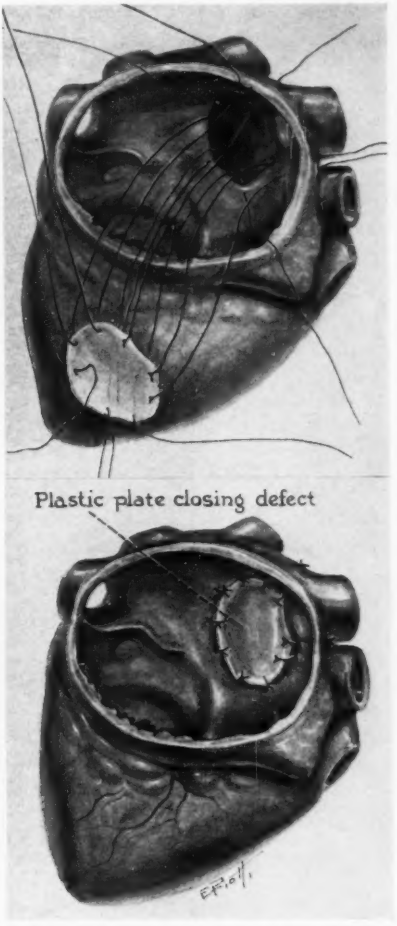

Fig. 6.—By working through a rubber "well" (here omitted for clarity) eccentric or very large septal openings can be closed by the onlay of polyethylene sheet, accurately sewed and anchored into place.

It is currently our practice to employ, whenever possible, the above listed Method 4 (Figs. 1 to 3). If this is not feasible because of the position or because of great size of a septal defect, we use Method 5 (Figs. 5 to 7).

Many patients with atrial septal defects have anomalous drainage of the pulmonary veins, particularly of those veins from the right lung. In rare instances

these enter the inferior vena cava, the coronary sinus, or particularly the superior vena cava; no method has yet been devised to cope adequately with such problems. Fortunately, most anomalies of pulmonary-vein drainage are such that the vessels enter the right auricle. We have found it rather easy and very effective to deal with

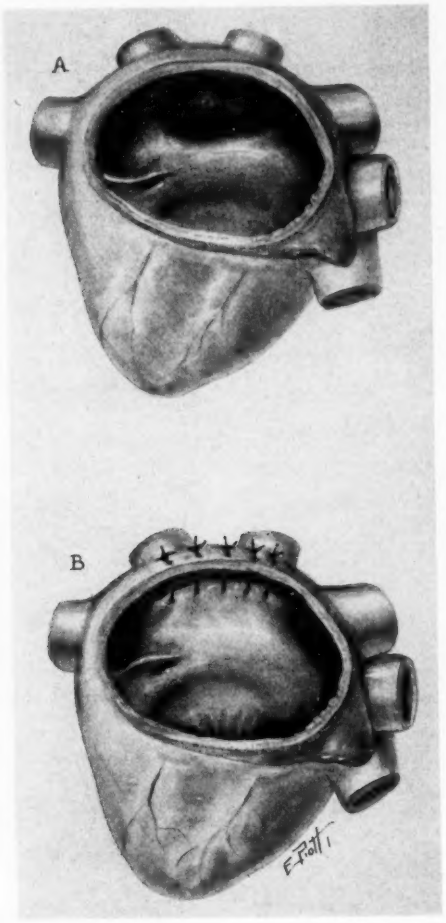

Fig. 7.—Method used for simultaneously treating an atrial septum defect and aberrant pulmonary veins which enter the right auricle. Mattress sutures of silk are employed to bring the leaf of septum snugged up to the posterior wall of the right auricle in a manner which effectively closes the septal opening and at the same time directs all pulmonary-vein blood into the left auricle.

these by the measures indicated in Figure 7 or in Figure 8. It is just as important to direct all pulmonary-vein blood into the left auricle as it is to abolish the communication between the two auricles.

RESULTS OF SURGERY

In our earliest attempts to close interauricular septal defects, three patients with very large apertures were subjected to the insertion of Hufnagel-type rigid lucite buttons (the mates of which could be screwed together) positioned on the two sides of the septum in such a way as to occlude the septal opening. There was insufficient septal tissue for these prostheses to grasp; each worked loose, and the patients died some days later.

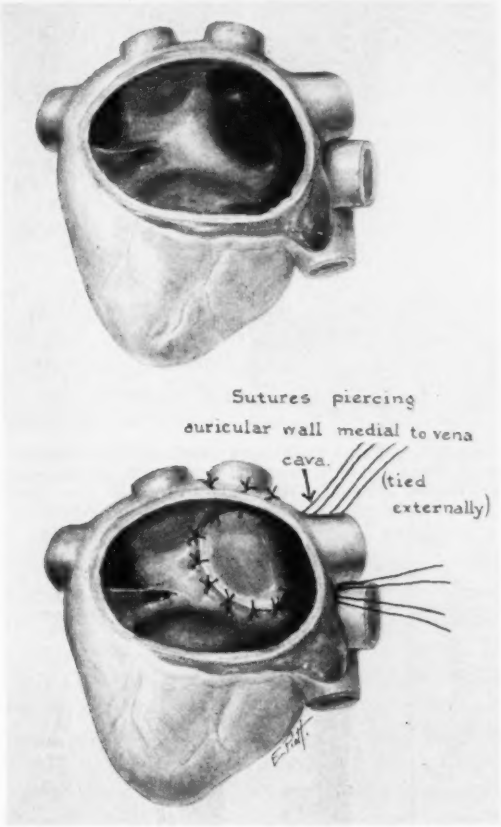

Fig. 8.—Method used for closure of a high posterior septal defect in which there are concurrent problems of directing all blood from the superior vena cava into the right auricle and also directing blood from an anomalous pulmonary vein into the left auricle. Proper placement and attachment of a polyethylene-sheet plate accomplishes the objectives simultaneously.

Twelve other patients, varying in age from 5 to 48 years, have been treated surgically by the methods shown in Figures 1 to 3 or Figures 4 to 6. Five of them died of various causes. Two of the fatalities occurred at the termination of operation, or later in the day thereof; they were almost certainly related to errors in defect closure or to insufficient replacement of blood which had been lost during operation. Such

fatalities should be preventable. Two deaths occurred a week after operation, when clinical and roentgenological features indicated that blood was damming up in the left auricle and pulmonary bed. At autopsy there was no mitral stenosis; presumably the left ventricle was unable to cope with the increased amount of blood being offered

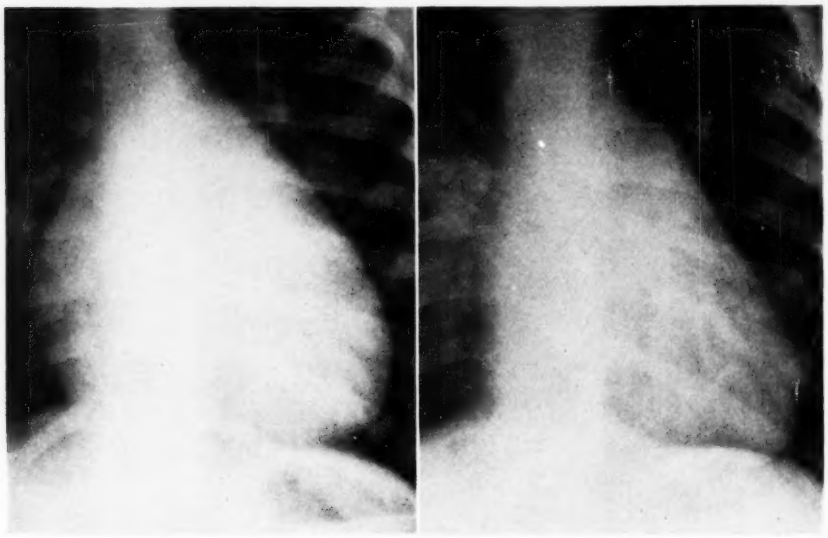

Fig. 9.—Roentgenograms, 7 ft. (2 m.), before (left) and after (right) surgical closure of an interauricular septal defect, showing reduction in size and alteration in shape of the heart. Right auricle, right ventricle, and pulmonary artery are smaller after operation.

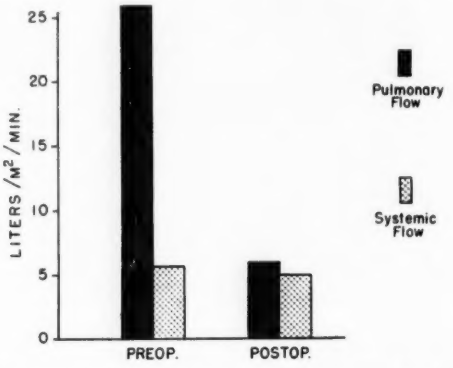

Fig. 10.—Physiologic measurements from catheterization studies on a 5-year-old girl, before and after surgical closure of a huge atrial septum defect. Comparison of preoperative and postoperative pulmonary flows indicates clearly that a tremendous burden has been taken off right ventricle. Equalization of pulmonary and systemic flows after surgery indicates that the septal opening has been completely closed by the operative procedure.

to it after surgical closure of the atrial septum defect. It is hoped that such disasters might be averted in the future by more careful handling during the critical period a week or two after operation (digitalization, reduction of blood volume, limitation of

salt ingestion, etc.). The fifth fatality occurred in a 38-year-old man who was known to have a very high pulmonary vascular resistance and a beginning reversal of flow through the septal opening (arterial oxygen saturation of 88%); good repair of the septum was accomplished, but exitus occurred as the chest was being closed. We now believe that such a situation is a contraindication to surgery.

There have been seven survivors. In four of these the septum was repaired by direct suture; in three others the opening was closed by the onlay of a polyethylene sheet which was sewed into place and anchored to the septum. In these seven cases, the postoperative courses have been most gratifying. The activity and forcefulness of the heart beats have been unquestionably reduced. Those who before had right-sided heart failure have now lost all evidence of this. The capacity for undertaking physical activity has been greatly augmented. In four, cardiac murmurs have disappeared, while in three a faint residual murmur can still be heard. Postoperative catheterization studies on four subjects show that in one a portion of the shunt remains, whereas in the other three the septum is now completely intact. (In the three most recent survivors, who have not yet been recatheterized, one was believed at operation to have well over 90% closure of a huge defect, and two were believed to be repaired perfectly.)

SELECTION OF PATIENTS FOR OPERATION

It is not necessary to operate upon all human beings who have an interauricular septal defect. The fear of future development of bacterial endocarditis does not justify operation, since it is known that the likelihood of having such infection is very slight, compared with the frequency of appearance of this complication with interventricular openings. Therefore indications for operation are almost entirely concerned with the increased work loads which an auricular shunt can place upon the heart. Small openings can be tolerated through a long and active life, the subject often surviving to advanced age with little or no symptomatology. On the other hand, larger openings produce left-right shunts of great magnitude, which greatly increase the work of the right ventricle and bring it to embarrassment or failure. Just where to draw the line between benign and burdensome forms is problematical. There can be no doubt that patients with prominent cardiac enlargement, with impressive pulmonary congestion, or with definite symptoms of cardiac embarrassment are headed for disaster even though it may be many months or even some years off; all of them should be operated upon. Concerning the patient who has no important symptoms but who by catheter study is found to have a left-right shunt of considerable size, it is our feeling that operation is advisable whenever the flow through the right ventricle (and lungs) is more than double that through the left ventricle (and peripheral system). This last statement represents our policy at the moment; it may have to be altered somewhat in the future as we learn more about the natural history of untreated atrial defects and as we gather further statistics regarding the risks of surgical closure of atrial openings.

Age, in itself, is not an important factor in determining operability, but at either extreme certain factors come into play which increase the technical difficulties of operation or which might compromise the results of surgery. In the first few years of life, smallness of the right auricle might hamper surgical manipulation on its interior. Beyond middle life, an exhausted myocardium or an existing thrombosis of

pulmonary artery radicles may make operation very hazardous. It is probable that the optimum ages for surgical repair of septal defects will be found in the range from 3 or 4 years up through the 20's.

A most important consideration when discussing the feasibility of surgery is the presence or absence of secondary vascular change in the lung bed. With the greatly augmented flow through the pulmonary circuit, arteriolosclerosis can appear, which, as it advances, increases the resistance in the pulmonary tree. This secondary change can progress to the point where blood dams up in the right side of the heart and even begins to produce a reversal of flow through the auricular defect. The shunt flow becomes right-to-left, manifesting itself by a fall of the peripheral arterial oxygen saturation, which, if of sufficient degree, produces cyanosis. Increased resistance in the pulmonary vascular bed can be recognized accurately by catheterization study, being reflected by appreciable rises in pulmonary artery pressure. High pulmonary pressure readings, when accompanied by only small increases in pulmonary blood flow, probably indicate that the risks of surgery will be great but not necessarily forbidding. (Swan [4] performed a successful operation when the pulmonary pressure was known to be 90 mm. Hg, and Bailey [1] has had a similar success after the pressure was known to be 120 mm. Hg.) However, if the secondary changes have advanced to the point where there is late onset of cyanosis (or diminished arterial saturation without appearance of cyanosis), operative closure of the septal opening will almost certainly result in fatality; we have had a surgical death in a 38-year-old man who had such a condition. In general, great rises in pulmonary vascular resistance are seen in older persons, but they are not necessarily related to the age of patients; we have found the resistance markedly elevated in an 8-year-old girl, and conversely, have seen it to be normal or only slightly elevated in some subjects beyond midadult life. Fortunately, the majority of patients with interatrial septal defects that we have studied have not had a high pulmonary resistance. (The late onset of cyanosis must be differentiated from the situation which is occasionally seen in a patient in whom there has been mild cyanosis from earliest life, the latter having a rather low pulmonary artery pressure and having cyanosis because of streaming of venous blood from a cava across a common auricle toward the orifice of the mitral valve.)

The presence of great cardiac enlargement, pulmonary engorgement, or right-sided heart failure is not a contraindication to operation. Each of these suggests a higher risk for surgical therapy but also indicates the urgent need for such treatment. While some patients with these desperate pictures will not stand a surgical ordeal, there is already ample evidence in survivors to show dramatic and beneficial effects on the heart and health when such crippled persons have had surgical treatment for the auricular shunt. In instances of this sort, where life hangs only by a thread, surgery should not be undertaken until every measure has been utilized to put the cardiovascular system in the best possible state; limitation of sodium intake may be desirable; the administration of digitalis and quinidine sulfate may be of help in controlling arrhythmias or improving cardiac action, and respiratory infection should be combatted, etc.

There can be no doubt about the necessity of performing cardiac catheterization studies on all subjects who are being considered for surgical treatment of a septal defect. Such investigation is important for the following purposes: (1) establish-

ing (or confirming) the diagnosis; (2) estimating the blood flow through the periphery, through the lungs, and through the shunt; (3) detection of any right-left shunting (diminished arterial oxyhemoglobin); (4) recognition of any anomalous drainage of the pulmonary veins, and (5) measurement of vascular resistance in the pulmonary bed. Only by such study can the physician adequately evaluate a patient's condition and express an opinion concerning the harmful effects or the possible benefits of surgical attack on the auricular abnormality.

SUMMARY

Small interauricular shunts can be tolerated by the human heart through a long life and, hence, do not require any surgical relief. Large interauricular shunts in which the pulmonary blood flow is twice (or more) that of the peripheral blood flow should be subjected to surgical closure of the septal opening. The methods which we prefer to use in accomplishing this repair are described herein. Postoperative observations on surgically treated patients have shown striking improvements in health and in cardiac function; physiologic studies have demonstrated marked reduction in the work of the right ventricle.

ABSTRACT OF DISCUSSION

DR. HENRY SWAN, Denver: Few men, if any, have made as many important contributions to cardiac surgery as Dr. Gross, and here again today he is to be congratulated for presenting this new and ingenious method of operating within the right auricle.

In 1913 Dr. Alexis Carroll described cardiac operations in general as being either open or closed, and Dr. Gross, I think, in his method has a little of both. Although the heart is open, the manipulations must be done under a flow of blood and therefore must be done by feel.

Now, what Dr. Gross has obtained, however, is very important, and that is time. The manipulations can be done deliberately while the blood flow continues.

For a number of years we have been interested in the problem of the technical aspects of the interauricular septal defects, and we have experimentally developed two methods which have since been clinically applied.

[Slide] The first consisted of inversion of auricular tips through septal defect. This illustrates a specimen experimentally similar to that shown by Dr. Gross.

[Slide] The next slide shows a postoperative specimen of the tube tips inverting through the septal defect. This method, although it was reasonably effective in the experimental animal, was given clinical trial, and although the patients tolerate the procedure well, we did not obtain good closure of the large clinical defects.

I think we did establish the principle of the Y-shaped lumen to the auricle; modifications of this method have been used clinically by both Drs. Kay and Baker. Because we did not close the defects well in the clinical patients, we took them back to the laboratory, and a second method was evolved, using a polyethylene button sewed across the septal defect and sewed to the inversion of the opposite side because we wished to be sure this intracardiac polyethylene button did not have a chance to become a foreign body in the heart.

[Slide] The results of this method were quite satisfactory, and this slide again shows the reaction that Dr. Gross showed us of the heart to polyethylene, and the smooth glistening surface.

This was also given clinical trial on two patients last year. In one of them the result was considered good; in the other, only fair, but I think it would have been a practicable method had we wished to pursue it. However, at this time we became interested in our laboratory in the attempt to develop a method of operating under direct vision with the open heart, and I think we have come some way toward accomplishing this by using the method first suggested three years ago by Dr. Bigelow, of cooling the patient and cutting off the circulation.

The important thing is to be able to prevent ventricular fibrillation as much as possible and also to be able to restore normal rhythm, should it occur.

In addition to this, it is important that air embolism be averted.

[Slide] We have been using a transverse incision crossing the sternum. This gives good exposure to all portions of the heart. The first step is to isolate the vena cava. Ligate the vagus vein, and then apply clamp, or first of all, pull up on the tapes. Allow the heart about a minute to empty itself. Put a clamp across the aorta and the pulmonary artery, and then it is possible to open the heart.

[Slide] The last slide shows an operative view. This is an experimental animal. In this instance of this operation it applies to the interauricular defect, and one has a situation not unlike this in the clinical patient.

We have given this method only very limited clinical trial. We have cooled seven patients with intracirculation for periods of from two minutes five seconds to eight minutes and a half.

We have performed an operation on the pulmonary valve in five of these patients and on the interauricular septal defect in two. There have been no deaths in this group, and all of the patients have apparently had a rather successful repair of the lesion for which they were operated on.

I think that if this can be done satisfactorily, it is important that we continue to explore the possibilities of operating within the heart under direct vision, because I think it is an important principle of surgery that when it can be done safely, it is desirable to see what we are operating upon.

Of all the methods we have tried for the repair of the interauricular septal defect, technically this direct-vision approach seems the preferable one. We have been fortunate, I think. Although the lesions (the holes) were very big, as Dr. Gross says, they were not, I think, over 1.5 or 2 cm. wide; consequently, we did direct-suture closure of those defects, but I would certainly agree with him that if the defect were any larger, it would be desirable to shove in a sheet of polyethylene, rather than to attempt to close it directly.

I should like to ask Dr. Gross if he meant to imply that if the pulmonary artery blood pressure were elevated he would recommend that that patient not be operated upon?

DR. GEORGE H. HUMPHREYS, II, New York: I do not know why Dr. Gross asked me to discuss his paper, unless it is that without any experience, I cannot possibly offer another method.

I want to echo Dr. Swan's admiration for Dr. Gross's contribution, not only for his previous contributions, but also for attempting to solve this problem of auricular septal defect closure. It is a challenging problem because, like the others, it presents a simple mechanical physiological defect, which theoretically should be curable by surgery and which, mechanically, Drs. Gross and Swan and others have been struggling with for quite some time.

It does seem as though we are now approaching the point where some sort of solution is at least in sight. There are several things, however, that trouble those of us who have not taken this problem to the laboratory, but have rather watched the developments from an admiring seat in the front row.

As Dr. Swan pointed out, there are essentially two methods, or a compromise between the two—a closed method, an open method, or a method which while open is still at least partly blind.

One has to use the finger instead of the eye. Dr. Gross's method and the method described by Dr. Schumaker more recently are both combinations. That is, they are not entirely blind like the inversion of the appendage which Bailey uses, yet they are not entirely open as just described by Dr. Swan.

Surely the wide open method has the greatest advantages from the point of view of technique, in terms of seeing what one is doing and knowing what one is accomplishing. It has, of course, the disadvantage of the necessity of preventing the circulation through the heart during that period and in some way making it possible for the patient to survive.

This can be done by cooling the patient, as Dr. Swan has described, or it can be done by use of an extra device, such as the one Dr. Gibbon has recently employed successfully. However, the trouble is that some of these things are very complex, complicated, and difficult to do.

They carry in spite of Dr. Swan's group or record, a considerable risk if we are going to think of them in terms of the results seen in the animal laboratory, where methods of that type are being developed, and one then has to balance and one has to face the facts. On the one side, what is the defect, and what is the effect of the defect if it is not operated on? On the other side, what is the risk of the procedure, and how effective can we expect that procedure to be?

We have been instructed at the Babies Hospital as to this balance. We have gone back into our records of auricular septal defects and found that at least in the Babies Hospital, practically all the children who had auricular septal defect had a very large defect. In the great majority of cases they had defects which did not resemble the experimental defects made in the laboratory, where a very nice round hole is present, and there is a lip all around which can be grafted in a suture or to which a piece of plastic material can be sewn.

Rather, they have been defects similar to the one shown in Dr. Gross's last picture, where there is an arc of atrial septum with no lip on one side, and more particularly, they have been the type of defect in which the backing lip is on the ventricular side against the septum, between the auricles and the ventricle, and often actually going down into the ventricle itself, so-called atrioventricular defect.

This is something which I do not think any of the methods described have the answer for. However, it is quite possible, and I should like to ask Dr. Gross whether he believes this to be true. Is it quite possible that such a defect—although it could not be wholly closed, I expect, by his method—could still be made so narrow that the defect would be changed from one which was an overwhelming physiologic disadvantage to one in which the physiologic disadvantage was relatively small?

The possibility, of course, exists that we have a lopsided view in looking at our autopsy records. Undoubtedly there are children who have gone through our clinic with auricular septal defects closable by Dr. Gross's technique, who have not come to autopsy.

What is going to become, or what has become, of those children? That, I can not answer. We do not know, and it is a very hard group of facts to unearth because these children become lost to follow-up when they grow up, and we do not know whether they later come to grief or not.

The problem then of what is the natural history of the auricular septal defect has to be taken into account. Certainly we have learned that in taking in these cases that if one can operate on the condition when the patient is relatively asymptomatic, that is the best time to do it. We now feel no hesitancy in doing that in those conditions because we know that while not every patient will die, many of them will, and because the mortality is low, perhaps ultimately that will be the case in the auricular septal defects.

I should like to ask Dr. Gross if he thinks that any auricular septal defect should be closed at this time or only those defects in which there is obvious borderline failure?

DR. CHARLES P. BAILEY, Philadelphia: I too, am an admirer of Dr. Gross's, both for his accomplishments and for his ingenuity, and I think the "well" is one of the most ingenious things I have ever heard of. However, as a result of my experience with Dr. Swan's technique in invaginating both atrial appendages in six cases and perhaps of both Dr. Cohen's report in 1947 and Dr. Dodrill's in 1950, on experimental bridging of the defect with an evaginated portion of the atrium, it finally occurred to me that the proper atrium to use was the right one, greatly dilated and redundant, whereas the left was of normal size, and being familiar with both the extracorporeal circulation and the hypothermia techniques, which I have been employing in animals, and the latter in human beings, I could appreciate how dangerous these methods were under certain conditions, and it seemed to me a closed technique might be better.

Since May, 1952, when we presented our first case, we have now operated on 29 patients with atrial septal defects by this technique.

Among these patients there were seven with analogous right pulmonary venous draining and three with mitral stenosis. Their ages ranged from 3 to 58 years. Most of our patients were adults, and the defects were up to 5 or 6 cm. in size in some instances. In all cases the defect has been closed either by the technique exactly shown or by a slight modification.

The ungloved left index finger is inserted, as Dr. Gross showed, through the right appendage and can readily make out the location, size, and lesions associated with the defect.

[Slide] This shows what one attempts to accomplish. With use of the index finger as a guide, the redundant right atrial wall is merely shoved into the perforated defect. When it is surrounded, the right atrium is changed to the shape of a doughnut and the defect bridged by atrial tissue.

Because of the redundancy of the right atrium, there is no interference with circulation apparently in these cases.

Of our 20 patients with a defect as shown, that is, a defect of the septum cecum abdomen, there were 2 who died. The others have done beautifully, and in eight patients in whom catheterization was done, the defect was completely closed in six. The other two had small residual defects. Perhaps I may have missed the secondary one.

In the nine patients with persistent ostium primum, there were four who died. One of them was a late death, and those deaths were not probably related to the technique, but rather to inexperience.

In one case I picked up the intercardiac aorta with needle and got an auricular fistula, which caused heart failure and late death. In another case in which we combined hypothermia with the closed technique, we got a standstill because of depression of myocardial contractility. In one other case we had a transfusion reaction of uremia.

I think the mortality seems unduly high even in that group. However, the death of those patients at least provided us with autopsy material to show that a defect of this type can be completely closed by invaginating and auricular wall.

Sometimes the defect is so large and sometimes there is no rigid tissue up above that is anterior, or toward the superior vena cava. Usually there will be a bit of tissue posteriorly, and perhaps some down above the valve.

In that case a doughnut should not be made of the right atrium but rather the wall sutured down in sort of a V shape. In other words, a new tunnel is created within the heart for the continuation of the superior vena cava, until the portion of the septum is reached which is just above the valve. Then that is continued around anteriorly so that the two vena cavae can communicate with the tricuspid valve. Of course, then the remainder of the right atrium can be left connected with the left, as long as the circulation is separated.

There was one other point I wished to make. In our experience, the advantages of direct vision for surgery, of course, are obvious, and yet, even in a clinic which is using hyperthermia and direct vision, which has been done in six operations under direct vision, as Dr. Swan described, in one instance, although the surgeons could see, they sutured the inferior vena cava into the left atrium in closing the defect.

I am not saying this facetiously because I did the same thing with use of the closed technique, and I had two other cases in which it could have easily happened if I had not had the previous experience and knew what to do.

That can happen even under direct vision. It is very unfortunate when it does happen.

Another unfortunate instance occurred in that same clinic; even though the operation was done under direct vision, they picked up the AP button going into the ventricle and did get a complete atrial-ventricular separation. I just say that to indicate that direct vision is not quite everything.

Dr. Robert E. Gross, Boston: To emphasize this problem of having to deal with afferent pulmonary veins in conjunction with closure and interauricular opening, I should like to show two ways in which we have handled it.

With a septal defect, as you can see, rather far posteriorly and with the veins from the right lung emptying into the right auricle rather than into the left, it is possible in closing the auricular defect to so place the sutures here, silk mattress stitches, taking those through the back wall to the right of the orifices of the right pulmonary veins; when the septum is dragged backward to the wall of the auricle one accomplishes two things, closure of the septal opening and also directing of the blood into the left auricle.

[Slide] This is another way of getting at this combined problem when there is a superior posterior defect, good rim, but very little tissue above or behind.

One has to deal with the orifice of the vena cava and also with the orifice of this superior vein, which is directed more toward the right into the left.

A plate is drawn into place here. It is easy to locate it and core it below and anteriorly.

Great care must be taken in the placement of the sutures posteriorly so that they run out the back wall. They can be directed to the right of the pulmonary vein, thereby directing the flow of blood from the vein into the left auricle, and here the superior part of the repair is done by running those mattress sutures out through the heart medial to the superior vena cava.

In all instances we put a tape around the vena cava before getting into the heart. We never know when we will run into this sort of thing, and one might want to raise the vena cava in the field so you can direct these needles out medially to the vena cava and bring this plate into the appropriate position.

To answer a few questions which were asked, Dr. Swan brought up the problem of what pressures in the pulmonary artery would be a contraindication to operation. We are feeling our way about this. I do not think any dogmatic statement can be made about this at this time, but in most of our patients the pulmonary pressure is up to 30 or 40 mm. Hg. When the pressure is as high as 50 mm. Hg, the patients still seem to tolerate the operation very well.

In the two subjects that died, the pulmonary artery pressure approximated that of peripheral arterial pressure, which is a good indication of high resistance in the pulmonary bed.

Dr. Humphreys asked what could be done about those youngsters who have the whole septum missing. I had no hesitation in believing that it is possible to sew in a foreign material like a plate and graft material, structures posteriorly, anteriorly. The big job comes down near the tricuspid valve.

I think it might be technically impossible by any method to anchor such a plate there, and as Dr. Humphreys suggests, I wonder if we can leave the curtain hanging free, unattached at the bottom, realizing that we do not have a perfect solution to the problem, but yet, we might be able to close off a great deal of the flow.

Last, Dr. Humphreys asked who should be operated upon. I feel very strongly that there are many small auricular defects that do not need surgery, that do not carry the risk of infection as ventricular septal defects do. They are small openings, a centimeter or less. Operation is not necessary in these instances.

I feel that only the larger defects should be tackled with the present knowledge of the surgery.

STENOSING TENDOVAGINITIS OF THE FOOT AND ANKLE

Studies with Special Reference to the Stenosing Tendovaginitis of the Peroneal Tendons at the Peroneal Tubercle

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STENOSING tendovaginitis of the foot and ankle is apparently considered uncommon. Actually it is not. The various forms of stenosing tendovaginitis which occur in the foot and ankle will be described.

A. TENDOVAGINITIS OF THE DORSAL TENDONS OF THE FOOT

The tibialis anticus, the extensor longus hallucis, and the extensor longus digitorum tendons lie under the cover of the ligamentum transversum cruris superiorly and the ligamentum cruciatum inferiorly. The fit of the tendon within the sheath is loose. The pedalling movement of the foot is more likely to give a peritendinitis crepitans of the tibialis anticus, movements of the foot provoking a dry creaking along the length of the tendon.

Stenosing Tendovaginitis of the Tibialis Anticus

Jagerink (1928) operated on a young woman with stenosing tendovaginitis of the tibialis anticus in whom the tendon sheath was thickened just above the ligamentum cruciatum. She was thereby cured.

A similar case is reported through the courtesy of Dr. Aaron Winderman.

Case 1.—A man, aged 61, fell down some steps on Sept. 4, 1948, injuring his right ankle. A painful, small, firm, round mass which moved with the tibialis anticus tendon was soon noted. A bloodless operation was done on Dec. 24, with the patient under general anesthesia. The sheath of the tibialis anticus was bulbous and thickened for an inch proximally to the upper edge of the transverse crural ligament. The mass disappeared under this ligament when the foot was plantarly flexed. The thickened sheath, adherent to the tendon, was split longitudinally and excised. The tendon then glided smoothly. Sections showed a thickened and highly vascularized sheath. He was well a month later.

Case 2.—I have seen an example of adhesive tendovaginitis of the insertion of the tibialis anticus in a woman 25 years old, which followed a minor crushing injury of the right foot, when a man stepped on her foot.

This distressingly painful malady demanded three periods of hospitalization and was only relieved by the resection of the scarred and adherent tendon sheath of the tibialis anticus. A slowly developing hemorrhagic bursitis at the insertion of the extensor longus hallucis was the effort sequel by incarceration of this tendon in the operative wound.

There is no report of stenosing tendovaginitis of the extensor longus hallucis in the literature.

Case 3.—*Adhesive tendovaginitis with loss of the power of dorsiflexion and abduction of the foot.*

A Nicaraguan seaman, 38 years old, whom I examined on May 25, 1951, was struck over the front of the left ankle on Jan. 13, 1951, by a sand box weighing 400 lb. (181 kg.), when his ship was suddenly tipped by a heavy sea. The time of contact was brief, a reverse tilt of the ship pulling the box away. He was at once unable to dorsiflex the dangling left foot.

He walked with a left drop foot. He could neither raise nor abduct the left foot by apparent absence of power in the tibialis anticus, the extensor longus hallucis, the extensor longus digitorum, and the peroneal muscles. He could not extend the toes. The tendons of the affected muscles showed continuity of their substance but were tender at the level of the ankle. The musculotendinous junction of the tibialis anticus was tender; so too was its insertion point. Passive motions of the left foot and ankle were free. The dorsalis pedis pulse was not felt, and there was anesthesia in the pedal distribution of the superficial and deep peroneal nerves and in the internal saphenous nerve. Roentgenograms of the left foot and ankle were negative for fracture and dislocation. The fourth metatarsal bone was congenitally short.

Operative exploration of the crushed tendons and nerves was advised. It is not unreasonable to believe that, as time went by, adhesion took place between the tendons and the covering annular ligament to give a secondary adhesive tendovaginitis which perpetuated his disability.

Cohen (1942) described a case of traumatic drop foot after a crush of the leg in which operation revealed transverse scarring in the belly of the tibialis anticus. The resection of this scar restored the power of dorsiflexion. This case is akin to mine, and although the level of injury was different, the effect was the same.

CASE 4.—*Early stenosing tendovaginitis of the distal end of the sheath of the extensor longus hallucis by direct blunt injury.*

A young woman, 22 years old, was seen on Sept. 22, 1951. She remembered vaguely that two months previously someone had stepped on the dorsum of her right foot in a crowded subway train. She seemed to have a simple contusion of the foot. Pain had been dull and constant. On three occasions there were sharp exacerbations of pain, each lasting up to half a day. On one of these occasions she could not walk and had to take meperidine (Demerol) hydrochloride. The pain did not radiate and was most intense over the upper part of the first metatarsal bone.

A slight swelling was found over the dorsum of the foot near the bases of the first and second metatarsal bones. The insertion of the tibialis anticus was tender. The important tender point was found over the extensor longus hallucis tendon near the upper part of the first metatarsal bone. An annular thickening was felt at the most distal part of the tendon sheath, where the tendon emerges from its sheath. Plantar flexion of the great toe (but not of its distal phalanx) induced pain at this point.

A diagnosis of stenosing tendovaginitis of the most distal part of the sheath of this tendon was made. Operation was done with the area under local anesthesia on Oct. 8, 1951. The tendon of the extensor longus hallucis showed no obvious stenosis, but its synovial layer was inflamed. The peritendinous tissue was thickened at the point of exit of the tendon from its sheath. An anomalous extensor tendon of the great toe was found medially to the extensor longus hallucis.

She was well on Nov. 9. The tendon of the extensor longus hallucis bowstringed a little more proximally than its left mate.

Winterstein (1930) reported the case of a woman, 37 years old, with stenosing tendovaginitis of the extensor longus digitorum (the extensor tendon of the second toe), not operatively confirmed. Six months before, she had broken the external malleolus of the right ankle. She complained of great pain on the dorsum of the foot at a point compressed by the leather band of her (half) shoe. The pain radiated up the leg, especially at night when the bed coverings touched the foot. Three fingers below the ankle joint and in line with the extensor tendon of the second toe, there was a little edema through which he felt a firm, tender, pea-sized swelling, just distal to the compressing leather band. Maximal extension and flexion of the foot gave pain.

B. STENOSING TENDOVAGINITIS OF THE MEDIAL TENDONS OF THE FOOT

The internal malleolus is the pulley for the tibialis posticus tendon and the flexor longus digitorum tendon. These two tendons and the flexor longus hallucis, whose pulley is the sustentaculum tali, are restrained by the ligamentum laciniatum.

There is no direct reference to the stenosing tendovaginitis of any one of these three tendons. The site of stenosis is more likely to be inframalleolar than retrotibial, though the latter is possible. The case reported by Kulowski (1936) was one of chronic purulent tenosynovitis and tendinitis of the posterior tibial tendon. Lipscomb (1944) reported examples of tenosynovitis of the tendons of the foot. Lapidus and Seidenstein (1950) discussed nonspecific chronic tenosynovitis (with effusion) about the ankle, the disease affecting the sheath of the flexor longus hallucis in one case and the sheath of the posterior tibial tendon in two cases.

Stenosing Tendovaginitis of the Posterior Tibial Tendon

A blunt direct injury on the inner side of the ankle contuses the tendon, or the tendovaginitis may be secondary to fracture of the internal malleolus. In compression injury the tendon is squeezed between the tuberosity of the scaphoid and the internal malleolus as the foot is suddenly inverted. It is therefore sometimes associated with tendovaginitis of the peroneal tendons in inversion injury. The tension injury or occupational stretching of the tendon by plantar flexion and eversion of the foot is unlikely, since such a movement is unnatural. The repeated active movement in dorsiflexion and inversion is likewise unnatural. Hence occupational tendovaginitis has never been recorded. I have seen several cases of tendovaginitis of this tendon by direct injury or by compression.

Case 5.—*Stenosing tendovaginitis of the posterior tibial tendon after fracture of the sustentaculum tali with operative confirmation.*

A church painter, aged 51, fell 18 to 20 ft. (5 to 6 m.) from a scaffold to a concrete floor on Dec. 21, 1948. Among other injuries, he fractured the sustentaculum tali of his left heel. Yet, even after the fracture healed, he tired easily. He could walk eight to nine blocks, and he found that going up a stepladder provoked pain lasting six hours, the pain radiating along the longitudinal arch of the foot.

The foot and ankle showed a free range of motion on Nov. 30, 1949, but sharp tenderness persisted along the line of the posterior tibial tendon just below the internal malleolus. The diagnosis of stenosing tendovaginitis of the posterior tibial tendon was confirmed when operation was done on Dec. 21. The sheath of the tendon was much thickened and adherent to the normal tendon for a distance of ½ to ¾ in. (1 to 2 cm.). The sheath was resected at the stenotic area and the ligament edges sutured loosely. The wound healed well. He had no complaints on Oct. 19, 1951.

The secondary development of tendovaginitis in the anomaly of calcaneonavicular synarthrosis or synostosis has not been previously recorded.

Case 6.—*Calcaneonavicular synarthrosis with secondary tendovaginitis of the dorsal tendons of the foot at the level of the ankle and with associated inframalleolar tendovaginitis of the flexor longus hallucis and flexor longus digitorum.*

A man, 43 years old, had fleeting sharp pain over the dorsum of his left foot for as long as he could remember. In the three weeks prior to my examination of him on Nov. 7, 1951, the pain increased both in intensity and in duration, became sharp and steady, and radiated up the front of the left leg. He limped and could not walk more than seven to nine blocks. The possibility of tendovaginitis as the source of pain was considered when tender points were found at the insertion of the tibialis anterior, over the extensor longus hallucis at the level of the ankle,

and over the inframalleolar course of the flexor longus hallucis, flexion of the great toe inducing pain in this latter site. There was little or no motion in the subtalar joint of each foot. Oblique roentgenograms of each foot disclosed calcaneonavicular synarthrosis. Axial views of each heel bone disclosed no abnormality in the joint the sustentaculum tali makes with the talus.

A bloodless operation done with the patient under general anesthesia on Jan. 17, 1952, showed that the sheath of the posterior tibial tendon was normal. The stenotic sheath of the flexor longus digitorum blocked the passage of a probe. Enough of this sheath was resected to allow the easy passage of the probe. The thickened sheath of the flexor longus hallucis was split for a distance of ½ in. but not resected since the probe could be passed easily. Comparable nonstenosing tendovaginitis was found in the thickened sheaths of the extensor longus hallucis, the extensor tendon of the fifth toe, and the peroneus tertius. The sheath of the tibialis anticus was normal. The split sheath of the extensor longus hallucis was loosely sutured to prevent bowstringing of its tendon. The inferior half of the sheath of the lateral extensor tendons was split. Of the seven tendons examined, one showed stenosing tendovaginitis and four nonstenosing tendovaginitis.

The inframalleolar wound separated to delay physical therapy. He was relieved of pain.

The primary defect, the developmental fault of calcaneonavicular synarthrosis, gravely restricted the movement of the subtalar joint. The tendovaginitis of the dorsal tendons of the foot followed the unconscious attempted supination of the rigid back foot. The tendovaginitis of the flexor longus hallucis and flexor longus digitorum was secondary to the gripping strain of the toes in compensatory pronation of the forefoot. The development of the tendovaginitis depends on time, for this malady is not seen in young persons with calcaneonavicular synarthrosis or synostosis.

C. Stenosing Tendovaginitis of the Lateral Tendons of the Foot

The Painful Peroneal Tubercle and the Stenosing Tendovaginitis of the Peroneal Tendons at the Level of the Peroneal Tubercle

I have divided the syndrome of the painful peroneal tubercle into the following two groups: (1) the painful peroneal tubercle which is congenitally enlarged, and (2) the peroneal tubercle painful by peroneal tendovaginitis, stenotic or not. The latter group is subdivided as noted below.

(*a*) The tension form of peroneal tendovaginitis by sprain of the ankle, including sprain fracture of the external malleolus and sprain fracture of the peroneal tubercle (inversion injury)

(*b*) Occupational or other strain of the peroneal tendons

(*c*) Peroneal tendovaginitis by direct blow

(*d*) Peroneal tendovaginitis by direct fracture of the peroneal tubercle in the inversion impact of an unusual sesamoid bone in the substance of the peroneus longus tendon at the level of the tubercle

(*e*) Compression tendovaginitis of the peroneal tendons at the level of the tubercle

(*f*) Peroneal tendovaginitis after fracture of the os calcis

(*g*) The painful peroneal tubercle as an early sign of rheumatoid arthritis

1. *The Enlarged Peroneal Tubercle.*—There are a number of papers which deal with the comparative anatomy of the peroneal tubercle and its variations of size and shape in the human being. Edwards (1928) examined 150 heel bones in human beings. The tubercle was prominent and well developed in 24%. It was a definite but less marked process in 20%, a low ridge in 14%, and absent in 42%. A good-sized peroneal tubercle was therefore found in only 44% of the heel bones examined

in human beings. The incidence of this tubercle given by other investigators cited by Edwards are almost the same: Gruber, 39.1% in the two sexes; Stieda, 33%; Pfitzner, 39.9% (of which 42% were in females and 39% in males), and Laidlaw, 36.5%. Oertl (1923 to 1924), who made a detailed study of the anatomy and comparative anatomy of this process, found the incidence to be 68% in the 75 heels examined. The strength of the peroneal muscles is not directly related to the size of the tubercle, for it may be poorly developed in big men. The knowledge of the incidence of this tubercle is important, since stenosing tendovaginitis occurs mainly in heels with well-developed peroneal tubercles.

Hyrtl (1860) found the peroneal tubercle to be so large in 3 of his 987 specimens that it lay in the same vertical plane as the external malleolus. A bursa covered the large process. The process is rarely so big that it seems to make the peroneal tendons run as in a canal. The tubercle is then a sustentaculum fibulae. Gruber in 1877, Francillon (1932) stated, found ossification of the sheath of the peroneus longus in this anomaly, the tendon running through a bony canal. He saw this four times in three skeletons of old people.

Francillon removed the peroneal tubercle twice. The enlarged epiphysis-capped left peroneal tubercle of a girl, 11½ years old, was resected under local anesthesia in December, 1931. (Pfitzner saw the epiphysis of the peroneal tubercle. Hasselwander [1909] examined 97 heel bones of patients between the ages of 13 to 24 years and in 5% found evidence of an apophysis of this tubercle, more or less fused). In Francillon's other case, the painful and enlarged left peroneal tubercle of a woman, 32 years old, was excised on Feb. 5, 1932, with resultant cure.

Budde (1924) reported on two patients with rigid flat feet with enlargement of the tubercle. The first of these patients was an old woman in whose left foot the peroneal tubercle articulated with the external malleolus of the fibula. Bonnet (1931) stated that the painful and enlarged peroneal tubercle was a consequence of a painful flat foot. The spasm of the peroneus longus made the tubercle *exubérant* to imprison the peroneus brevis between the external malleolus and the tubercle. He found a synovitis of the peroneal tendons in a female cook with painful flat feet and a very large peroneal tubercle. She was relieved by arch supports. Polosson (1931), who discussed Bonnet's paper, resected the large osseous beak of the tubercle in a 22-year-old woman with such sharp pain in her right foot that she could not walk. The beak made a tunnel for the peroneus brevis tendon as it turned toward the external malleolus. The opened sheaths of the peroneal tendons were normal. A thin free tendinous tongue derived from the peroneus brevis tendon in the region of the hyperostosis was resected. His second patient was a 20-year-old woman with flat feet whose right foot showed a very large tubercle. She was given arch supports.

CASE 7.—*Congenital enlargement of the peroneal tubercle as one of a series of fibular-sided anomalies.*

A 7-year-old girl had a series of minor defects of development along the fibular side of each leg. The fibular heads were high. A loose discoid external meniscus which locked the left knee was removed on May 4, 1948. Each external malleolus was prominent. The left peroneal tendon luxated a little on inversion of the foot, but this corrected itself later spontaneously. The left peroneal tubercle was enlarged. On each side an anomalous extensor tendon ended on the styloid process of the fifth metatarsal bone. The peroneus tertius tendon was well seen on each side.

CASE 8.—*Acquired enlargement of the peroneal tubercle.*

The left peroneal tubercle of the paralytic foot of a young hospital dietitian was considerably larger than the tubercle of the normal right foot. The left foot showed a cavovarus deformity with severe metatarsal equinus. The peroneus longus muscle was strong, the tibialis anticus muscle weak.

The peroneal tubercle is the fulcrum, or hypomochlion, of the peroneus longus. It is not unreasonable to believe that the peroneal tubercle gradually enlarged to meet the demand of this dominant muscle.

2. Stenosing and Adhesive Tendovaginitis of the Peroneal Tendons.—Stenosing tendovaginitis of the peroneal tendons takes place at the fulcrum of the peroneal tubercle. There is reasonable expectation of similar tendovaginitis at the other two turning points of the tendon, the external malleolus and the cuboid.

Hackenbroch (1927) operated on two middle-aged patients, one a man and the other a woman. Both had a painful sensitive thickening of the peroneal tendon sheath just below the tip of the external malleolus. The inferior peroneal retinaculum was thickened and the peroneal tendons imprisoned by the rigid sheath. Woltereck (1927) described the condition of a waiter, 48 years old, who complained of pain in his right foot on standing and on walking. A pea-sized firm swelling was found in the course of the peroneal tendons 1 cm. below the tip of the external malleolus. At operation on Nov. 15, 1925, a chronic inflammation of the peroneal sheath was found, the thickened sheath compressing the tendons distally. The peroneus brevis tendon forked 5 cm. from its insertion. Timmer (1928) who discussed Jagerink's paper, stated that he had encountered a case of stenosing tendovaginitis of the peroneal tendons in which the condition had been relieved by nonoperative treatment. The exact location of stenosis was not given. Liavaag (1945) reported stenosis of the peroneal sheath in a woman, 54 years old, who presented an inframalleolar mass 3 by 1 cm. in size. This condition was operatively confirmed.

Aberle-Horstenegg (1932) described five cases with pain localized to that point in the course of the peroneus longus tendon where it passes under the cuboid bone. The roentgenogram showed the absence of an os peroneum in each case. He believed the malady to be a tenosynovitis of the peroneus longus tendon in the sole of the foot. It was relieved by conservative treatment. Brun (1939) reported the case of a woman, 33 years old, in whom, after a sprain of her ankle, pain developed under the first metatarsal near the insertion of the peroneus longus. She could not walk, so great was the pain. The sheath was injected with procaine hydrochloride near the styloid process of the fifth metatarsal, over and at the insertion of the tendon, to give immediate and maintained relief.

Tendovaginitis of the peroneus longus in association with a painful multipartite os peroneum was described by Lapidus and me in 1931.

The cases reported by Hildebrand (1907) and by Vischer (1919) are not examples of stenosing tendovaginitis of the peroneal tendons. Hildebrand examined a young officer with bilateral luxation of the peroneal tendons with sheath changes which were not stenotic. In Vischer's patient, who had rheumatoid tenosynovitis of the peroneal tendons, a warm, red, fluctuating swelling, the size of the palm of a hand, was found over the external malleolus.

Peroneal tendovaginitis at the level of the peroneal tubercle has not been reported in the literature. The inversion injury which stretches the peroneal tendons to give

this delayed stenosis exerts maximal tension effect at the peroneal tubercle. A significant tension relation exists between the length of the peroneal tendons and the length of the peroneal tubercle. The tubercle is more or less equidistant from the external malleolus and the cuboid but is more laterally placed than the malleolus. The length of the tendon is constant in the given subject at a given time. The tubercle, which bends the tendon, gives it neutral or physiologic tension with absence of slack. The more lateral position of the tubercle or its physiologic equivalent, hypertrophy of the tubercle, increases the bend of the tendon and hence its tension. On the other hand, the more medial position of the tubercle or its absence lessens tension, the probable physiologic accommodation being increased tone of the peroneal muscles (Fig. 1).

The sudden inversion which gives increase in tension stretches the tendons and their sheaths and thrusts them strongly against the os calcis, since the angle of bend of the tendon is suddenly increased. The strain of the ankle is manifest sooner than the stretch injury of the ensheathed tendons. In time the irritated sheath thickens to give either stenosis or adhesion at the level of the tubercle. Sometimes

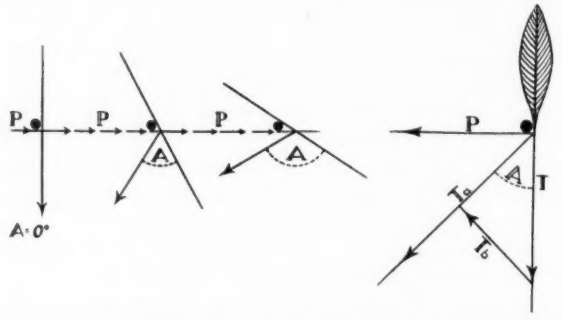

Fig. 1.—Right, *T* is the tension force which pulls the tendon around the pulley, *P*. The force is resolved into two components, *Ta* giving pull and *Tb* stabilization against the pulley. As the angle *A*, the angle of bend of the tendon about the peroneal tubercle, increases, *Ta* lessens. Left, lateral displacement of the pulley, *P*, given constant length of tendon, is equivalent to increase in the angle *A*.

minor avulsion fractures follow the inversion injury, such as avulsion of a tiny fragment from the external malleolus or from the tubercle itself, which may break by pull of the calcaneofibular ligament. The tendons do not tear. Peroneal tendovaginitis is rarely occupational. It may follow direct injury. In all cases the objective constants were swelling and tenderness over the peroneal tubercle and painful restriction of inversion of the foot. The other findings, the objective variables, are derived from associated conditions, sprained ankle, broken heel, etc. I have encountered at least 25 to 30 cases of this malady, in 6 of which operations were performed.

The operative incision is placed on the outer side of the heel. At its longest it extends from the tip of the external malleolus to the styloid process of the fifth metatarsal. The peroneal tubercle is at its approximate center. Avoid the lateral dorsal cutaneous nerve which is the continuation of the sural nerve. The thickened fibrous septum of the retinaculum is resected after the fibrous sheath is opened and resected. The peroneal tubercle is cleared and the tendons and their mucous sheaths inspected. Only the subcutaneous tissues and skin need be closed.

The Forms of Peroneal Tendovaginitis: (*a*) Tension form of peroneal tendovaginitis and ankle sprain.

CASE 9.—*Operation for stenosing peroneal tendovaginitis after severe inversion injury of the foot.*

A painter, 48 years old, fell on Nov. 22, 1944, from a stepladder placed on a sloping driveway. His inverted right foot caught between the two parts of the ladder. He was treated for a sprain fracture of the ankle. He limped and could walk only three blocks on June 19, 1946, and he tired quickly. He could not go up ladders. The peroneal tubercle was tender and swollen and inversion of the foot a little restricted. The lower part of the belly of the peroneal muscles was tender. The roentgenogram revealed irregularity of the dorsal part of the scaphoid and adjacent talar head and a spur on the internal malleolus.

Operation on July 8, 1946, demonstrated a moderate thickening of the peroneal sheath at the peroneal tubercle. The peroneal tendons were somewhat thickened. The sheath was resected. The thickened sheath showed fibrocartilaginous transformation.

The dorsal lateral cutaneous nerve, which is the terminal part of the sural nerve, was unfortunately cut; consequently, sensation was lost over the bases of the fourth and fifth toes. The neuroma was resected on May 17, 1947.

He was seen last on July 12, 1948. He had been working as a painter both on level ground and on ladders for many months. He began climbing ladders on Jan. 15, 1948. He did not limp and could walk 15 to 20 blocks. The tubercle was not tender, and inversion of the foot was slightly restricted. There was slight hypesthesia of the dorsolateral part of the foot.

CASE 10.—*Sprain fracture of the peroneal tubercle by tear of the calcaneofibular ligament with operative resection of the stenotic sheath of the peroneal tendons.*

A 55-year-old plasterer fell 6 or 7 ft. (1.8 or 2.1 m.) from a plank placed on two ladders, on July 31, 1944, while plastering a ceiling. He turned his left ankle in, breaking it. The ankle was still weak and swollen on Oct. 5, 1945. He could not walk more than five blocks or go up ladders or walk down steps easily. There were still tenderness and swelling of the outer side of the ankle, with some restriction of its movements. Both inversion and eversion of the left foot were restricted. The roentgenogram taken on Oct. 12 disclosed slight hypertrophic changes in the articular end of the tibia. A small bone fragment had been torn from the tip of the peroneal tubercle and was displaced superiorly somewhat (*a post hoc* interpretation). The articular surface of the anterior half of the subtalar joint was irregular in outline and sclerotic. The bones of the foot and ankle showed moderate osteoporosis.

The painful peroneal tubercle was recognized on Nov. 26, for swelling, pain, and tenderness now concentrated there. At operation on Dec. 14, the tubercle was exposed after the sural nerve was seen. The much thickened fibrous coat common to both peroneal tendons was split. A probe passed both distally and approximally met the obstruction of the stenotic sheath. The synovial lining of the tendon was hyperemic and hyperplastic. The thickened sheath was resected.

He had no pain on Oct. 16, 1946. He could walk 2 miles (3 km.) without fatigue on any terrain, and he could go up and down steps and ladders. The motions of the foot were not restricted, but he still had slight swelling and tenderness over the peroneal tubercle. He had no trouble at all with the foot on Oct. 25, 1948.

(*b*) Occupational or other strain of the peroneal tendons.

CASE 11.—A 50-year-old woman used both feet at the same time to pedal a machine making woolen jackets. She averaged 20 pedal movements per jacket and made 600 such movements per day. The left foot became "achy" on July 1, 1948. A year before she had found "lumps" in both heel cords.

The left peroneal tubercle was a little swollen and tender and inversion of the foot somewhat restricted on July 21, 1948. Each tendo achillis showed an oval swelling in its substance, with its long axis in the line of the tendon. Each swelling began about 1 in. (2.5 cm.) from the insertion of the tendon and extended proximally an inch. The maximal width of the tumor was ½ in. She walked with a slight heel limp and could stand on tiptoe.

The peroneal tendovaginitis followed the repeated movement of the left foot in plantar flexion and inversion. The swelling of each heel cord is probably an old partial rupture with hemorrhage into the substance of the tendon by the repeated movements in plantar flexion, although the possibility of xanthoma must be considered.

The swelling of each heel cord was lessened by the salutary effect of physical therapy, but on Feb. 18, 1949, slight swelling and tenderness still persisted over the peroneal tubercle.

CASE 12.—*Peroneal tendovaginitis after the repair of a peroneal hernia.*

A woman, 56 years old, was struck on the outer side of the left leg on Feb. 15, 1947, by a stick attached to a shoe rack. The resultant peroneal hernia, located at the point where the superficial peroneal nerve emerges from the deep fascia, was operatively closed on May 14, 1949. The existence of a mild tendovaginitis of the peroneal tendons at the peroneal tubercle was quite evident on Jan. 25, 1949. The tubercle was not large. Inversion of the foot was limited. This tubercle has remained painful (July, 1951) despite the injection of procaine into it and the use of heat.

(*c*) Delayed peroneal tendovaginitis after a direct blow about the ankle.

CASE 13.—A department of sanitation worker, 50 years old, was hit on the outer side of the right ankle by the crank of a sand spreader on Feb. 5, 1948. He walked with a heel limp on Feb. 9. There was considerable swelling, slight ecchymosis and tenderness over the external malleolus and below it, and some restriction of foot and ankle joint motions.

He could walk five blocks on June 1, 1948. There was still swelling and tenderness on the outer side of the ankle. Then there was found greater tenderness and some swelling over the peroneal tubercle. The inversion of the foot was moderately restricted, and dorsiflexion of the ankle was only 100 degrees. He walked with a heel limp. He was not fully well on Dec. 8, 1948, for he still had slight swelling and tenderness on the outer side of the ankle but none over the tubercle.

(*d*) Ununited fracture of the peroneal tubercle with extensive secondary adhesive peroneal tendovaginitis and discovery of a hitherto undescribed sesamoid bone in the substance of the peroneus longus near the peroneal tubercle.

CASE 14.—A man, 56 years old, twisted his left ankle on a steel-bar reenforced flooring on June 28, 1948. The resultant pain and swelling persisted. The ankle felt weak. The outer side of the ankle was still swollen on Feb. 14, 1949, with most tenderness and swelling located over the prominent peroneal tubercle. Inversion of the foot did not exceed 10 degrees and eversion, 25 degrees. Ankle and midtarsal joint motions were normal. He walked with a left heel limp and on the outer border of the foot. Roentgenograms disclosed an apparently ununited fracture of the peroneal tubercle (Fig. 2*A*).

Operation was done on Feb. 26, 1949. The sheath of the peroneal tendons, especially at the level of the peroneal tubercle, was tremendously thickened and adherent to the peroneal tendons from the external malleolus to the styloid process of the fifth metatarsal bone. It was fully resected between these two bony landmarks. The surface of the tendons was a little irregular and less shiny than normal. The anterior and inferior part of the peroneal tubercle was the site of an ununited fracture. This ununited piece of bone was removed. Palpation, and then the slitting of the tendon of the peroneus longus beneath the tubercle, showed that its bulk was filled by an oval sesamoid bone about ½ in. long and ¼ in. wide. The impact of this bone against the tubercle as the foot inverted broke the tubercle. The sural nerve was not injured (Fig. 2*B*).

On Nov. 13, 1951, he stated that "the foot was not bad." He could walk more than 20 blocks but still found irregular ground troublesome. He was working in a coffee warehouse as a warehouseman. Although he limped a little, he could walk and stand tiptoe. The very large peroneal tubercle was tender. Inversion and eversion of the foot were slightly restricted. There was vague numbness of the dorsolateral side of the foot.

This hitherto undescribed sesamoid bone in the substance of the peroneus longus tendon is not an os peronaeum.

(*e*) Compression tendovaginitis of the peroneal tendons.

The sudden abduction of the foot which breaks and sometimes avulses the internal malleolus, may compress the peroneal tendons between the peroneal tubercle and the tip of the external malleolus.

CASE 15.—A 19-year-old girl fell down two steps in a dark hallway on May 3, 1946, when her right heel caught on the edge of a step. Among other things she had an abduction injury of the right foot which broke the internal malleolus and the lower end of the fibula in the oblique manner consistent with the abduction arc of movement. As time went by, she complained of pain over the femoral origin of the internal lateral ligament of the right knee and

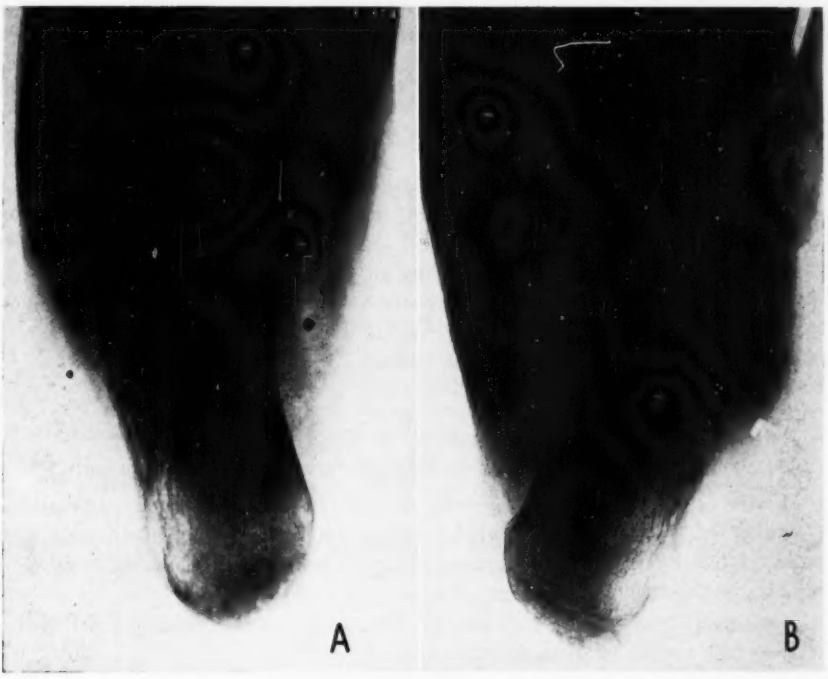

Fig. 2.—*A*, there is nonunion of the peroneal tubercle in its anteroinferior part. The impact of a sesamoid in the substance of the peroneus longus at the level of the peroneal tubercle broke the tubercle and produced an extensive adhesive peroneal tendovaginitis. This is the preoperative roentgenogram taken on Feb. 25, 1949. *B*, postoperative roentgenogram taken on Oct. 5, 1949, after the resection of the ununited fracture of the peroneal tubercle. Print is reversed. This hitherto undescribed peroneal sesamoid bone is seen as an oval body just lateral to the peroneal tubercle.

over the peroneal tubercle of the right foot. The internal malleolus, united by fibrous tissue and not by bone, was not tender.

The peroneal tubercle and the internal lateral ligament were explored on June 24, 1948. The presumed cyst under the origin of the internal lateral ligament was not found. The peroneal tubercle was of good size. Its fibrous sheath was thickened. The peroneal tendons were normal. The tubercle was cleared of its fibrous coat. The operations relieved her of pain, and on Feb. 28, 1949, she had only slight tenderness over the peroneal tubercle.

(*f*) Pain over the peroneal tubercle in heel fracture.

CASE 16.—*Compression fracture of the os calcis with secondary peroneal tendovaginitis as the cause of persistent pain and operative resection of a scarred sheath.*

A bridge painter, 51 years old, fell 18 ft. on July 5, 1945, and landed on his heels. He broke his right heel bone and the first lumbar vertebra. The roentgenograms revealed a badly comminuted fracture of the os calcis with a normal tuber angle. The broken bone healed well in plaster. Tenderness over the peroneal tubercle was first found on Dec. 3, 1945. He still had variable pain and swelling on the outer side of the right foot on June 10, 1946, located over a thickened and tender peroneal tubercle. The palpation of the tubercle imparted a sense of fluid to the finger. Peroneal hernias were found on each side. Inversion of the foot was painful and restricted.

Operation was done on July 8, 1946. The subcutaneous tissues were thin and scarred. The outer surface of the peroneal sheath was scarred and thickened, obscuring identification of the tendons. That part of the sheath attached to the tubercle was opaque white and measured 3/16 to ¼ in. (0.48 to 0.64 cm.) thick. This sheath was resected. A probe then passed up the peroneal sheaths easily. The peroneal tendons were covered by joining the edges of the split retinaculum loosely. Microscopic study of the sections showed a thickened and abnormally vascularized tendon sheath.

On July 21, 1948, he had occasional pain in the foot and sometimes swelling. There was a slight swelling below and posteriorly to the external malleolus. The inversion of the foot was still restricted.

(*g*) The painful peroneal tubercle as an early sign of rheumatoid arthritis. A painful peroneal tubercle is sometimes seen as an early sign or harbinger of rheumatoid arthritis, an observation twice made. On the other hand, the peroneal tubercle was not significantly tender in a young woman, 23 years old, with bilateral rheumatoid tenosynovitis of the medial and lateral tendon sheaths of each ankle.

STENOSING TENDOVAGINITIS OF THE FLEXOR TENDONS OF THE TOES IN THE DIGITAL SHEATH

Lewin (1941) stated that trigger toe, a condition like trigger finger, follows the stenosing tendovaginitis of the digital sheath of the flexor tendons of the toes. His patient, a ballet dancer, could not bend the big toe because of a stenosing tendovaginitis of the flexor longus hallucis.

I have seen two patients with presumptive stenosing tendovaginitis of the flexor tendons of a toe but have no operative proof.

SUMMARY

Described in this paper are the various forms of stenosing tendovaginitis which occur in the foot and ankle. The stenosing tendovaginitis of the peroneal tendons at the peroneal tubercle is not uncommon and may often be the cause of obscure or persistent pain after an injury to the ankle.

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INTUSSUSCEPTION DUE TO MECKEL'S DIVERTICULUM

Review of the Literature from 1933 to 1951 and Report of Nine Cases Seen at St. Louis Children's Hospital

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A SURVEY of the literature reveals a wide difference between the classical type of acute intussusception and that initiated by Meckel's diverticulum. To determine the nature, extent, and explanation of these dissimilarities, all cases of the Meckel's diverticulum type of intussusception in the English-speaking literature since Harkins' [1] original report in 1933 have been reviewed. The disparities were found to pertain to age incidence, symptomatology, clinical and surgical findings, and mortality.

Our interest in this subject was stimulated by a relatively high incidence of Meckel's diverticulum in a series of 116 cases of acute intussusception [2] and by the high morbidity and mortality in these particular cases. Some manifest differences between adult and pediatric patients in the Meckel's diverticulum variety of intussusception are outlined by a brief presentation of nine cases of this syndrome seen in St. Louis Children's Hospital from 1934 to 1951.

PREVIOUS OBSERVATIONS

Intussusception is not a common complication of Meckel's diverticulum. Wellington,[3] reviewing the literature on diseases of Meckel's diverticulum, found 326 cases up to 1913. Only 59, or 18%, of these were cases of intussusception. Greenwald and Steiner [4] limited their review in 1931 to the pediatric age group. They found reports of 47 cases of Meckel's diverticulum and added 4 cases of their own. In 5 of these 51 cases, 9.8%, intussusception occurred. In a pathological study of 63 cases of Meckel's diverticulum in children reported by Christie [5] in 1931 none were complicated by intussusception. Of the 73 cases of Meckel's diverticulum in infancy and childhood presented by Ladd and Gross,[6] 17, or 23.2%, were complicated by intussusception.

Likewise the incidence of Meckel's diverticulum in acute intussusception is not high. Of 2,414 cases of intussusception collected from reported series by Harkins [1] only 2.5% were associated with Meckel's diverticulum. In 25,149 routine necropsy reports collected from various sources by the same author the incidence of Meckel's diverticulum was 1.3%. Gross and Ware [7] found 29 cases of Meckel's diverticulum in their series of 610 cases (4.7%).

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The incidence of Meckel's diverticulum in 116 cases of acute intussusception in St. Louis Children's Hospital from 1934 to 1951 inclusive was 9.4%. In only 9 of the 11 cases did the diverticulum act as the apex of the intussusception.

In an extensive review of the literature up to 1933 Harkins [1] found 160 cases of intussusception associated with an invaginated Meckel's diverticulum and added 2 cases of his own. Since Harkins' review there have been 52 reports of intussusception associated with Meckel's diverticulum. Twenty of these were in the foreign literature. The remaining 32 reports comprised a total of 37 case histories. These are indicated in the list of references.* Cases 9 (Bunch [16]) and 12 (Martin [19]) are examples of simple invagination of the diverticulum without intussusception of the small bowel and are not included in the following analysis.

ANALYSIS OF THIRTY-FIVE CASES OF INTUSSUSCEPTION DUE TO MECKEL'S DIVERTICULUM REPORTED FROM 1933 TO 1951 WITH COMPARISONS OF PREVIOUSLY REPORTED CASES AND CASES OF ACUTE INTUSSUSCEPTION

Age and Sex.—Intussusception associated with Meckel's diverticulum is more likely to be seen in older patients. Harkins [1] found the average age in 113 cases to be 13.1 years. Only six patients in his series were less than one year of age. In the 35 cases published since Harkins' [1] report all but 2, or 94.2%, of the patients were over 2½ years of age. Twenty-one, or 60.0%, were over 10 years of age. The average age was 17.2 years. These figures are in marked variance with the age at which ordinary intussusception takes place, approximately 80% of the latter occurring before 2 years of age.

Eighty per cent of the patients were males. This figure corresponds closely to that published by Harkins [1] (79%) and is not unlike the sex incidence of acute infantile intussusception.

Symptoms and Signs.—With reference to symptoms, it is of interest to note that in Case 9 (Bunch [16]), one of the two cases of simple invagination of Meckel's diverticulum without intussusception of the small bowel, there were no abdominal complaints whatsoever. During laparotomy for gynecological reasons a mass was found in the ileum. On resection this proved to be an inverted Meckel's diverticulum. This observation may serve to explain the relatively incipient nature of the intestinal obstruction and strangulation in intussusception due to Meckel's diverticulum. Certainly primary simple invagination of the diverticulum from a localized area of the bowel wall should not cause the same degree of circulatory impairment seen in intussusception of the entire circumference of the bowel. It is possible that such uncomplicated invagination may have been present in some of the less critical episodes in the past history of many of these patients. This premise, plus the apparent advantage of an older age group, seems to offer the only reasonable explanation for the striking difference found between acute intussusception of infancy and intussusception precipitated by Meckel's diverticulum in adults with respect to the relative lack of an obvious surgical emergency in the latter. The appearance of shock or apathy so striking in acute intussusception in infancy was alluded to in only 11 cases and it is noteworthy that in all but 2 of these cases the patients were less than 15 years of age.

Abdominal pain of varied degree was present in all cases on admission. Vomiting was present in 30 of the 35 cases.

* References 8 through 39.

A palpable abdominal mass was present in well over 70% of reported cases of acute intussusception. Its presence in the Meckel's diverticulum type of intussusception is less common. In 22, or 62.8%, of the cases in our review an abdominal mass was recorded. Not infrequently it was described as indefinite, recurrent, or of inconstant location.

Attention has been drawn to the rarity of progression of these intussusceptions beyond the hepatic flexure. A priori the mass when present is most likely to be found in the right lower quadrant of the abdomen. In Harkins' review, of the 49 tumors with data concerning location, 41 were palpated in the right lower abdominal quadrant. Of the abdominal tumors present in this series, 54.5% (12 cases) were present in the right iliac fossae. None was present in either upper abdominal quadrant and only one was described in the left lower quadrant of the abdomen. In four cases the mass was palpated per rectum. In no instance in this review and only twice in Harkins' [1] larger series was the apex of the intussusception palpated within the rectum. The latter finding is common in the ordinary type of acute intussusception in infants and children, constituting 19% of our recently reported series.[2]

Melena, one of the characteristic symptoms of acute intussusception in infancy and childhood, is relatively infrequent in the Meckel's diverticulum type of intussusception in the older age group. In Harkins' review 43 patients had melena, 34 did not have it, and for 37 no data were submitted. In the present series only seven patients, or 20%, passed blood by stool, enema, or on rectal examination.

Fuchsig [40] believed that the infrequency of melena was the result of a tamponade effect of the inflamed and edematous Meckel's diverticulum within the lumen of the intestine. In considering this reduced incidence of melena, one must keep in mind the older age of the patient with this particular type of intussusception. Braun and Wortmann,[41] reporting on melena in ordinary intussusception, found an incidence of 94% in children under 2 years of age, 62% in older children, and only 38% in adults.

In view of the high incidence of irreducible or gangrenous intussusception (13 of the 35 cases, 37.1%) this infrequency of melena is all the more perplexing. In our recent review of 116 cases of intussusception in infancy and childhood there were only 17 cases (14.6%) with gangrenous or irreducible bowel, and yet melena was a prominent symptom in 80.1% of the cases.

Duration of Symptoms and Past History of Abdominal Complaints.—As noted by Harkins [1] originally, chronicity of symptoms made it very difficult to determine the exact onset of the present illness. In 46 cases (40.3%) in his series there had been a history of similar abdominal complaints suggesting previous attacks. The average symptom duration in Harkins' [1] review was 81.6 hours. This suggests a clinical picture of less critical nature than that seen in young infants with acute intussusception.

Of the 35 patients in our survey 19, or 54.2%, had had previous abdominal complaints of pain with or without vomiting. The total duration of these intermittent symptoms varied from several days to 12 years prior to admission. Seven patients (20%) had been hospitalized previously, six of them for similar complaints of abdominal pain and one for massive intestinal hemorrhage. Three of these patients were discharged, and four had abdominal operations.

In three additional cases reference to previous laparotomy was made. In none of these seven cases with previous laparotomy was any mention made of a Meckel's

diverticulum. Two of the cases deserve special comment. In case 32 (Pool and Porter [35]) "tubes were removed and a tumor of the intestine infolded." On reexploration four months later an ileocolic intussusception to the ascending colon was found with the surgically "infolded" Meckel's diverticulum acting as the apex of the intussusception. In case 31 (Feggetter [34]) an ileoileal intussusception was found and easily reduced. Appendectomy was performed "in the hope that further attacks would be prevented." In this case it is possible that the Meckel's diverticulum was not involved in the original ileoileal intussusception. On reexploration one month later there were three distinct intussusceptions separated from each other by several inches of bowel, one of these containing the invaginated diverticulum.

All of these cases reemphasize the need to search for a Meckel's diverticulum in all laparotomies. Such exploration is mandatory when there is no significant disease of the appendix or pelvic viscera to account for the patient's preoperative symptoms. The almost constant location of the diverticulum within the terminal three or four feet of the ileum makes such a search feasible.

Operative Findings.—In contradistinction to the ordinary intussusceptions in which the ileocecal and the ileocolic types predominate, the majority of the intussusceptions (28 cases, 80.0%) were ileoileal or enteric. Ileoileal intussusceptions are most commonly seen in the older patient and are frequently associated with an obvious source of origin, such as polyps, tumors, Meckel's diverticulum, or congenital stenosis. It seems logical that such intussusceptions remain enteric by virtue of the barrier of the normal ileocecal valve to the greater bulk of the intussusceptum when it contains an invaginated space-taking lesion.

Of the seven cases of ileocolic or ileoileocolic type, intussusception had progressed to the ascending colon in six, and to the midtransverse colon in one. This is in keeping with the clinical findings and the infrequency of a mass being present in the left half of the abdomen or palpable per rectum (within).

There was one instance [34] of multiple intussusception—two of the ileoileal type and one ileocolic. In this case the patient had a past history of two previous hospital admissions for similar complaints. An ileoileal intussusception had been reduced surgically on the first admission, and on the second admission a recurrent intussusception was presumably reduced by barium enema.

There was one case [25] complicated by a preoperative 360-degree volvulus of the small bowel in addition to the ileoileal intussusception.

Operative Procedures.—Twenty-two, or 62.8%, of the intussusceptions were viable and were reduced manually by taxis. Of the 15 intussusceptions with viable Meckel's diverticulum, 13 were resected and 2 were left undisturbed. In one of the latter cases [28] extreme abdominal distention and the critical condition of the patient precluded any further surgical procedure. In the other case,[12] that of an infant aged 5 months, the surgeon planned to remove the Meckel's diverticulum and the appendix when the child was three or four years of age. There were seven instances in which the diverticulum alone was gangrenous or irreducible. In all these resection was done—most commonly with a segment of the adjacent ileum—and followed by end-to-end anastomosis.

Eight of the intussusceptions were gangrenous and five were irreducible, the total comprising 37.1% of all the cases. This figure closely approaches that reported by Harkins [1] in 1933, in which 37 of 108 cases of the Meckel's diverticulum type

of intussusception were complicated by gangrene of the bowel. Such a high incidence of gangrenous or irreducible intussusceptions is undoubtedly due largely to delay in proper diagnosis before and after hospital admission. Of these patients, 46.01% had symptoms for 72 hours or longer prior to surgery. Three patients had symptoms of 24 hours', three days', and four days' duration on admission but were not operated on for another two, five, and six days, respectively.

Operative procedures in the 13 cases with gangrenous or irreducible bowel were as follows: Exteriorization of gangrenous bowel in 1 case, resection with end-to-end or side-to-side anastomosis in 10, and resection with enterocolostomy in 2 cases. In one of the latter cases, No. 11 (Stuppel [18]), a lateral enterocolostomy had originally been performed without resection. Because of increasing pain and temperature, reexploration was done. At this time there was obvious gangrene of the intussuscepted loop; this was excised, leaving the original anastomosis intact.

Nine appendectomies were performed, one in the presence of gangrenous bowel. None of these cases was fatal.

Pathological Examination of Meckel's Diverticulum.—Of the 33 surgical specimens of Meckel's diverticulum in this review, pathological examination was reported in 19. Nine of these, or 47.3%, showed gastric mucosa. In one of the latter specimens [11] sections showed partial replacement of the gastric mucosa by a Grade II adenocarcinoma. There was one case [29] which showed a submucous lipoma. In a few specimens the degree of gangrene precluded accurate histological diagnosis.

Mortality.—In Harkins' [1] original review of all recorded cases of the Meckel's diverticulum type of intussusception up to 1932, of 112 cases 41% were fatal. This figure was considerably higher than that found for intussusception not due specifically to Meckel's diverticulum. Harkins [1] attributed this discrepancy to delay in proper diagnosis, with surgery performed "only as a last resort." This impression of high mortality has persisted and was quoted as late as 1945! However, a review of the literature (in English) from Harkins' [1] report up to and including 1951 has shown a dramatic decline in mortality to 2.8%. Of the 35 cases reviewed in this paper only one was fatal, Case 24 (Atwood [28]). This was that of an 8-year-old child who on admission appeared "lethargic and cyanotic." Duration of symptoms was 48 hours. The ileocolic intussusception was manually reduced and found to be viable. Death occurred one hour postoperatively. Permission for autopsy was not granted.

Since the incidence of gangrenous and irreducible bowel in this review is actually higher than that published by Harkins almost 20 years ago, the precipitous decline in mortality is apparently due to improved preoperative, surgical, and postoperative care. The persistently high incidence of gangrenous intussusception points to the need for the awareness of this syndrome, with earlier diagnosis and corrective surgery.

ANALYSIS OF NINE ADDITIONAL CASES OF MECKEL'S DIVERTICULUM TYPE OF INTUSSUSCEPTION IN INFANCY AND CHILDHOOD

An analysis of nine cases of the Meckel's diverticulum type of intussusception (Table) seen in St. Louis Children's Hospital from 1934 to 1951 shows that whereas the findings in some aspects conform to those found in adults, in others there is a striking and important difference.

Nine Cases of Meckel's Diverticulum Type of Intussusception in Infancy and Childhood

Case No.	Age, Yr.	Sex	Symptoms	Duration of Symptoms Hr.	Past History of Abdominal Complaints	Abdominal Mass	Operative Findings and Procedures	Pathological Condition of Meckel's Diverticulum	Outcome
1	4/12	M	Pain, vomiting, melena; "obtunded"	72	.....	0	Ileoileocolic intussusception to hepatic flexure—viable, reduced; Meckel's diverticulum at apex	Gastric mucosa	Died 5 hours postoperatively; volvulus 180° of small bowel
2	8	M	Pain, vomiting, melena; "toxic"	144	Copious rectal hemorrhage at 23 mo. of age	Present inconstantly	Ileoileal intussusception, gangrenous, resected with end-to-end anastomosis; Meckel's diverticulum in intussusception	Pancreatic tissue plus gastric mucosa	Died 8 hours postoperatively
3	3	M	Pain, vomiting; "unresponsive"	72	.....	Present in right lower quadrant	Ileoileal intussusception originating in Meckel's diverticulum; bowel gangrenous resected with end-to-end anastomosis	Architecture completely destroyed	Died 10 hours postoperatively
4	3/12	M	Vomiting, melena; "stuporous"	48	.....	Present in right upper quadrant	Ileoileal intussusception originating at Meckel's diverticulum; bowel reduced; Meckel's diverticulum gangrenous, excised with ileum, end-to-end anastomosis	Gangrenous	Died 48 hours postoperatively
5	11/12	M	Pain, vomiting, melena; "knocked out"	24	.....	0	Ileoileocolic intussusception to splenic flexure, originating in invaginated Meckel's diverticulum; intussusception reduced, viable; Meckel's diverticulum irreducible, resected	Acutely inflamed	Recovered
6	1 11/12	M	Pain, vomiting, melena	48	.....	0	Ileoileocolic intussusception to cecum, originating in Meckel's diverticulum, gangrenous, resected with colostomy (Mikulicz)	Hemorrhagic, necrotic	Recovered
7	9	M	Pain, vomiting, melena	48	"Stomach ache off and on for several years"	Suprapubic	Ileoileal gangrenous intussusception, originating in Meckel's diverticulum; bowel resected with end-to-end anastomosis plus ileostomy	Necrotic	Recovered
8	4/12	M	Pain, vomiting, melena; "listless"	72	.....	Right upper quadrant	Ileoileocolic intussusception to transverse colon, originating in Meckel's diverticulum, viable, reduced	.....	Recovered; postoperative intestinal obstruction due to adhesion band
9	6/12	F	Pain, vomiting, melena; "toxic"	72	.....	Left side of abdomen	Ileoileocolic intussusception to splenic flexure, originating in Meckel's diverticulum, viable and reduced manually	.....	Recovered

Four of the nine patients (44.4%) in the group with the Meckel's diverticulum type of intussusception were over 23 months of age. This age distribution is in keeping with reports of intussusception complicated by Meckel's diverticulum, and, as mentioned previously, quite unlike the age incidence of the classical type of intussusception.

Two of the nine patients had had previous abdominal complaints. In one of these there had been a copious rectal hemorrhage six years previously and the other patients had complained of "stomach ache off and on for several years." The presence of melena and "shock," which was relatively infrequent in the published adult cases, was a common finding in these pediatric patients.

Four of these intussusceptions were ileo-ileal or enteric, and five were ileoileocolic. Four of the latter had progressed beyond the cecum but none beyond the splenic flexure. This confirms the impression that space-occupying lesions acting as the apex of an intussusception are most commonly retained within the ileum; presumably the ilocecal valve acts as a barrier to the added bulk of the intussusception. In the older age group the incidence of ileoileal intussusceptions in which Meckel's diverticulum is involved is even higher, 80% in the present review.

Of greater interest is the apparent added risk of Meckel's diverticulum. This impression has been expressed by several authors. Oberhelman and Condon [42] recognized the presence of a Meckel's diverticulum as a definite mortality factor. Of their six cases patients with the Meckel's diverticulum type of intussusception, four required resection (66.6%) and three died (50%). In Ladd and Gross's presentation of 73 cases of pathological complications of Meckel's diverticulum 16 deaths were reported. Seven of these deaths, or 43.7%, were due to intussusception of the diverticulum, whereas the incidence of such intussusception was only 23.2%.

In four of our nine cases (44.4%) there was gangrene of the intussusception. Since the incidence of gangrenous or irreducible bowel in 107 cases of acute intussusception [2] in which Meckel's diverticulum was not present as the apex of the intussusception was only 11.2%, the added morbidity in the Meckel's diverticulum type of intussusception is quite apparent.

This arresting incidence of gangrenous and/or irreducible bowel is also seen in the cases of the Meckel's diverticulum type of intussusception reported in the literature. In 37 of 108 cases in Harkins' series (34.2%) and in 37.1% of the 35 cases reviewed in this report the intussusception was found to be gangrenous and/or irreducible. Whereas the duration of symptoms undoubtedly plays a major role in the increased incidence of gangrenous bowel, the presence of the diverticulum itself must in some way contribute to this increased morbidity. If, as Fuchsig [40] suggested, the diverticulum acted as a tamponade to prevent melena, one can theorize that this same pressure could increase bowel strangulation and necrosis.

Four of the nine patients listed in the table died, a mortality of 44.4%. The mortality in 107 cases of ordinary acute intussusception [2] not initiated by a Meckel's diverticulum was only 5.6%. Since the time element is comparable in these two fatal groups the increased risk in the Meckel's diverticulum type of intussusception in infancy cannot be ignored.

In the 35 cases of Meckel's diverticulum intussusception since Harkins' review the mortality rate was only 2.8%. The much higher mortality (44.4%) in Meckel's

diverticulum intussusception in infants and young children must be attributed to the hazards of youth, since the cases in other respects were comparable. All of the nine patients whose cases are summarized in the table were less than 10 years of age, whereas 60% of the patients in our report † were over 10 years of age.

SUMMARY AND CONCLUSIONS

An analysis of 35 previously reported cases of the Meckel's diverticulum type of intussusception reveals many differences from ordinary acute intussusception.

1. Whereas the majority of acute intussusceptions occur before one year of age, those associated with Meckel's diverticulum are most common in the adolescent or older patient.

2. The appearance of "shock" or apathy, so characteristic of acute intussusception, was seldom noted in the older patients with Meckel's diverticulum intussusception.

3. An abdominal mass is less constantly found in intussusception due to Meckel's diverticulum. Since the majority of these intussusceptions remain enteric or seldom progress beyond the hepatic flexure, the mass is usually found on the right side of the abdomen. Rectal intussuscepta are rare in Meckel's diverticulum intussusceptions.

4. The decreased incidence of melena has been partly attributed to the tamponade effect of the intraluminal Meckel's diverticulum and in an undetermined manner to the older age of the affected patients.

5. About half of the patients had a past history of similar abdominal complaints. Twenty per cent in the reviewed series had previous laparotomies without detection of the Meckel's diverticulum.

6. In contradistinction to ordinary intussusceptions, the majority were ileoileal, presumably owing to the barrier of the ileocecal valve to the added bulk of the space-taking Meckel's diverticulum.

7. The continued high incidence of gangrenous bowel was attributed to delay in correct diagnosis. This was apparently fostered by the subcritical nature of symptoms, which we postulate could be due to preliminary invagination of the diverticulum prior to intussusception of the small bowel.

8. The fall in over-all mortality in Meckel's diverticulum intussusception from 41% in 1933 to 2.8% at present is a tribute to the advances in preoperative, surgical, and postoperative care.

Nine additional cases of the Meckel's diverticulum type of intussusception in infants and children are presented. Characteristically these showed an older age incidence, previous abdominal complaints, and a high incidence of enteric intussusceptions.

Of greater significance was the increase in morbidity and mortality in infantile intussusception complicated by Meckel's diverticulum. The incidence of gangrenous bowel in these nine cases was 44.4%, compared with 11.2% in 107 cases of intussusception without Meckel's diverticulum. The mortality of 44% compares unfavorably with 5.6% in 107 cases of intussusception without Meckel's diverticulum.

† References 8 through 39.

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BENIGN TUMORS OF THE AMPULLA OF VATER

Comparison of Survival Following Local Resection of Benign and Malignant Ampullary Tumors

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THE RADICAL operation of pancreatoduodenectomy is the procedure of choice for carcinoma of the ampulla of Vater. The nature of cancer warrants this serious operation in spite of its high mortality and in spite of the fact that the operation may produce permanent nutritional disorders in the surviving patient.

It is obvious that such a hazardous procedure should not be used as the surgical treatment of benign ampullary tumors. It should be possible to cure such tumors with a simple local transduodenal resection. This advice, simple in execution and logical in theory, is seldom followed in practice because the accurate histological differentiation between benign and malignant ampullary tumors is difficult, and not always possible from frozen sections taken at the time of operation.

The first object of this presentation is to point out the existence of benign tumors of the ampulla of Vater and the microdiagnostic difficulties they may present. The second object is to compare the survival times following local excision of benign and malignant ampullary tumors.

Even though the benign tumors of the ampulla of Vater are not common, they do occur with greater frequency than one may suspect. Baggenstoss,[1] in a study of the autopsy material at Mayo Clinic up to 1936, found 25 cases of polyps of the papilla, as compared with 28 cases of primary carcinoma of the same region. Other series, however, contradict these findings. Gröbl and Pohl[2] found 214 cases of carcinoma and only 1 single instance of papilloma of the ampulla of Vater among 2,630 autopsy cases in which a clinical diagnosis had been made of calculi or inflammatory disease of the extrahepatic bile ducts. Shapiro and Lifvendahl[3] found 3 benign and 12 malignant tumors of the extrahepatic biliary tract in 2,500 autopsies.

Moore, McElwee, and Romiti[4] state that they encountered about 52 cases of benign tumors of the bilary tract in the survey of the literature. To this should be

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added two cases reported by Cattell [5] and one case of ours described in this article. The total number of reported benign biliary tract tumors is therefore 55. These include benign tumors of the extrahepatic bile ducts, the ampulla, and the papilla of Vater. Actually, only 12 cases of benign tumors of the ampulla of Vater are noted in the literature.

Christopher [6] reports the incidence of various forms of benign tumors of the lower part of the common duct and the ampulla of Vater as follows:

Papilloma and polyp	16
Adenoma	16
Lipoma	4
Fibroma	2
Neuroma	1
Granuloma	1
Melanoma, benign	1
Carcinoid	1

Only six of these tumors definitely involved the ampulla. A study of the literature discloses further that the diagnosis of a tumor at the ampulla of Vater is rarely made correctly before operation or before necropsy in spite of striking early symptoms presented by the biliary obstruction. Sharpe and Comfort [7] reviewed 40 cases of obstruction of the common bile duct due to carcinomas or other tumors and found that in all but 1 case the correct diagnosis prior to operation was missed.

Small tumors within the duodenum are difficult to detect even at the time of operation. Lieber, Stewart, and Lund [8] have called attention to the fact that 32% of tumors of the ampulla were not recognized at the time of duodenotomy. The pathologist is confronted with a similar diagnostic problem. The histological patterns of benign and malignant changes may be extremely difficult to differentiate. Wills and his associates [9] state that the cross section of small pancreatic ducts within the papilla of Vater may present themselves as packets of small ducts and foci of the pancreatic tissue between the muscle fibers in the duodenal wall, thus mimicking an invasive tumor.

The diagnostic difficulties encountered at celiotomy may be illustrated by our own experiences in connection with three cases of ampullar tumors. In all three cases the exploratory findings were distended gall bladder and common duct. In two patients the tumor of the ampulla was palpable through the duodenal wall; in the third case the tumor was not found until the duodenum was opened and the ampulla brought into view. This experience indicates rather forcefully the necessity for duodenotomy in instances of negative exploratory findings in patients with obstructive jaundice. This is particularly imperative when the gall bladder and the common duct are distended and the extra-ampullary obstruction has been ruled out in the process of exploration. It is logical to carry this thought a step further and

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stress the wisdom of routine duodenotomy on all ampullary tumors, whether they are palpable at exploration or not. Upon exposure of the tumor a biopsy may differentiate a benign tumor from a malignant one. With this simple procedure, patients with a diagnosable benign tumor would be saved from the radical operation of pancreatoduodenectomy. A similar thought is expressed by Cattell and Pyrtek [5] in their recent article describing two cases of benign ampullary tumors.

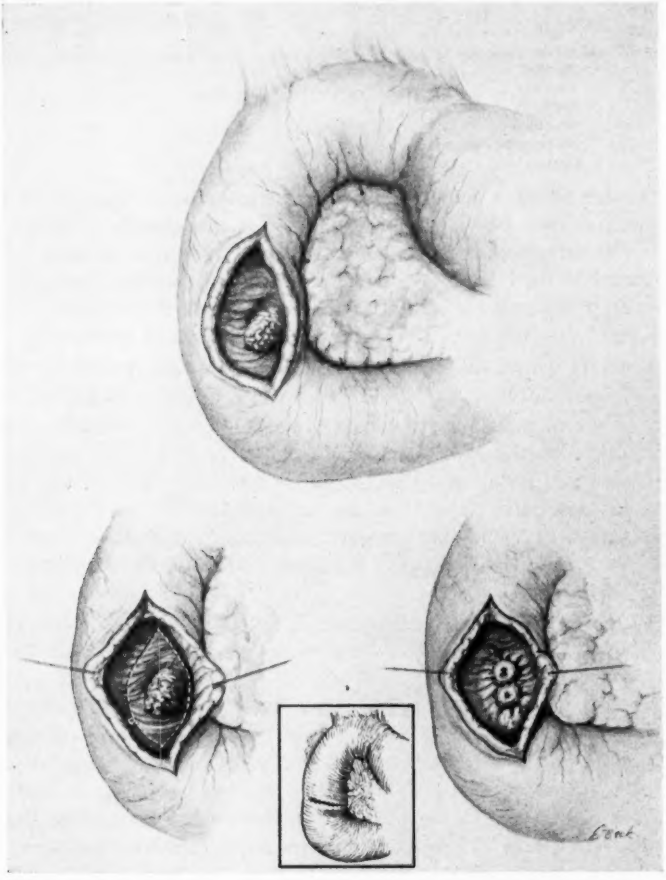

Fig. 1.—Local excision of tumor of ampulla of Vater, with transplantation of common and pancreatic ducts.

CASE 1.—A man aged 44 was first seen in January, 1940. His principal complaint was jaundice of four months' duration. He had no pain, nausea, vomiting, or diarrhea. The physical and laboratory examinations suggested the diagnosis of obstructive jaundice, probably due to calculus in the common duct or to carcinoma of the head of the pancreas or the ampulla of Vater.

At operation the gall bladder and the common duct were found greatly distended. The ampulla of Vater contained a tumor measuring 2 cm. in diameter. The tumor was exposed by a longitudinal incision in the duodenum and excised locally by an elliptical resection of the pos-

terior duodenal wall. The transected common and pancreatic ducts were reimplanted into the posterior wall of the duodenum. This procedure is illustrated in Figure 1. The patient made an uneventful recovery and is alive today, 13 years after his operation.

The histological diagnosis of the tumor removed was an adenocarcinoma arising from the common-duct portion of the ampulla of Vater. The long survival of the patient following a local excision stimulated our curiosity to reexamine the tumor microscopically. Upon reexamination the tumor revealed itself as a benign intraductile papilloma.

CASE 2.—An x-ray diagnosis of tumor of the ampulla of Vater was made. This was possible because the patient was seen after an abdominal exploration at another institution. The tumor was not recognized, and therefore the biliary obstruction was treated by T-tube drainage of the common duct. Radiopaque material injected through the T-tube visualized a defect at the ampulla, which was interpreted as a tumor.

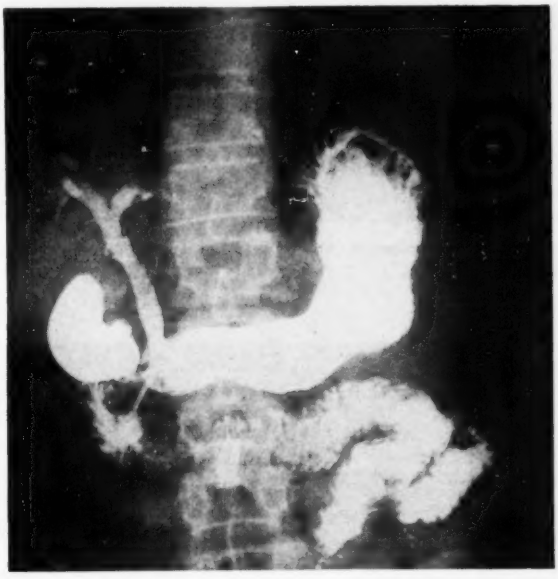

Fig. 2 (Case 1).—Roentgenogram. Barium has entered the distended common and hepatic ducts. Narrowed common duct shows patent anastomosis with the duodenum. Cholecystoduodenostomy used as a safety measure is visible owing to the filling of the gall bladder with barium. Roentgenogram was taken 11 years after surgery.

At operation, performed by Dr. Dallas B. Phemister, a tumor measuring 2 cm. in diameter was found in the ampulla of Vater. The same type of local excision as that described and illustrated in the first case was performed. The patient had an uneventful recovery. He lived in good health and died of metastases 11 years after his operation. The histological diagnosis was an invasive carcinoma of the ampulla of Vater.

CASE 3.—The patient was a woman, aged 52, whose only complaint was a silent jaundice of two months' duration. At celiotomy the gall bladder and the common duct were found distended but free from stones. Repeated palpation of the duodenum failed to detect a tumor in the ampulla. When the duodenum was opened longitudinally, a small firm tumor was felt in the papilla. This tumor measured 2 mm. in diameter. A simple local resection with transplantation of the ducts was performed by Dr. Prohaska. This patient died four and one-half years later of extensive carcinoma metastases.

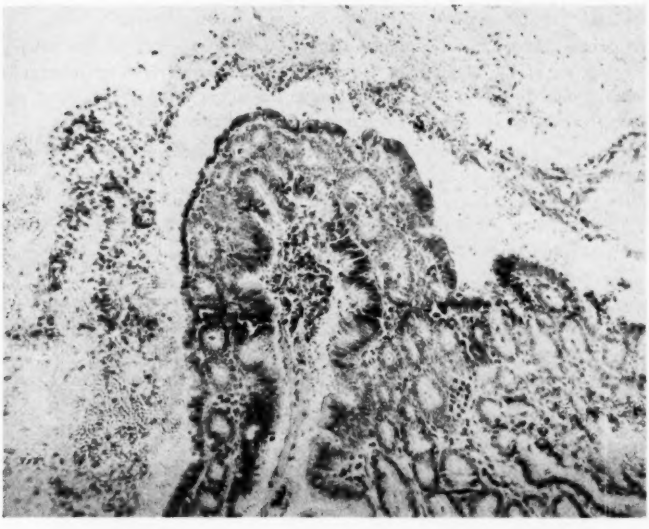

Fig. 3 (Case 1).—Photomicrograph, low power, showing benign intraductile papilloma of ampulla of Vater.

Fig. 4.—Higher magnification of Figure 3.

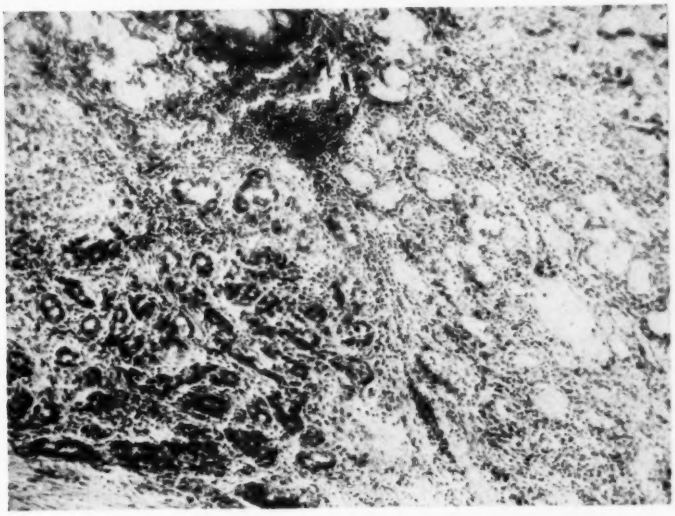

Fig. 5 (Case 2).—Photomicrograph, low power, showing adenocarcinoma of ampulla of Vater.

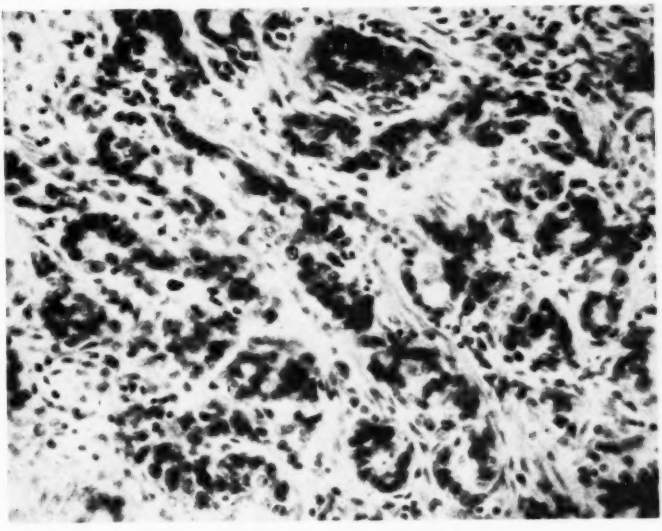

Fig. 6.—Higher magnification of Figure 5.

COMMENT

Local transduodenal resection with transplantation of the common and pancreatic ducts appears to be an adequate operation for a benign tumor of the ampulla of Vater. This contention is supported by the long survival of our first patient. Even the second patient, whose tumor was a definite carcinoma, survived 11 years after a local excision. The third patient, who also had a malignant tumor which measured only 2 mm., survived four and one-half years. It is plausible to reason that this patient might have been cured by a pancreatoduodenectomy.

SUMMARY AND CONCLUSIONS

The experience with these cases and the survey of the literature led us to formulate the following conclusions:

1. Histological differentiation between benign and malignant tumors of the ampulla of Vater is difficult to establish at the time of operation.

2. The differentiation between benign and malignant tumors of the ampulla of Vater should be attempted by direct inspection and biopsy accomplished through duodenotomy.

3. If a histological diagnosis is made at operation, then local transduodenal resection of benign tumors of the ampulla of Vater would be a welcome substitution for the radical procedure of pancreatoduodenectomy.

A case of proved benign tumor in which the patient survived 13 years after local resection is presented.

Two cases of long survival following local resection of a carcinoma of the ampulla of Vater are noted.

AN INVESTIGATION OF EFOCAINE, A LONG-ACTING LOCAL ANESTHETIC AGENT

I. Animal Studies

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UNTIL recent years, surgery was frequently accompanied with considerable discomfort and misery. Developments in the field of anesthesia have decreased these reactions appreciably. There still remains, however, the problem of postoperative pain. Parenteral administration of narcotic drugs, at present, is the principal method of solution of this problem. Side-reactions of these drugs, such as nausea, emesis, bowel distention, respiratory depression, suppression of the cough reflex, mental disorientation, vasomotor hypotension, and allergic manifestations, have led those investigators interested in this problem into the field of long-lasting local anesthetic agents. These investigations have proceeded along two main lines. The first attempts sought agents which, in themselves, produced prolonged anesthesia. Such drugs as absolute ethyl alcohol, benzyl alcohol, quinine salts, and compounds of the insoluble aminobenzoate series proved to have too great a local or systemic toxicity. The other method of prolonging local anesthetic action was the addition of a substance that would slow the absorption of the anesthetic agent. Oil bases have been utilized for this purpose. However, these produce undesirable local tissue reactions, such as cysts, foreign-body granulomas, and, occasionally, nerve injury.

Recently, a new long-acting local anesthetic, Efocaine,[1] was introduced into the field of medicine.[2] Efocaine consists of the following anesthetic agents: butyl-*p*-aminobenzoate, 5%; procaine, 1%, and procaine hydrochloride, 0.25%. The first two agents, crystalline, slowly absorbed substances, insoluble in water, are brought into solution by a solvent consisting of propylene glycol, 78%; polyethyl-

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Drs. C. R. Stephen and Ruth Martin, of the Division of Anesthesia, and Dr. Wiley Forbus of the Department of Pathology, gave encouragement during development of this material; Mr. Phillip Picket prepared the microscopic material, and Mr. Carl Bishop did the photography.

1. The Efocaine and Efocaine solvent were supplied by E. Fougera and Company, Inc., New York.

2. Ansbro, F. P.; Iason, A. H.; Shaftel, H. E.; Halpern, A.; Latteri, F. S., and Bodell, B.: The Development of Efocaine: A New Approach to Prolonged Local Anesthesia, Anesthesiology **13**:306, 1952.

ene glycol 300, 2%, and distilled water, 20%. Upon injection the crystalline anesthetic substances are deposited as the solvent material is absorbed.

In this paper are reported the results of experimental animal studies on the action of Efocaine. The following paper reports parallel clinical tests of this material.[3] These two papers constitute an enlargement of studies previously presented by one of us.[4]

PROCEDURES

The following materials were investigated: Efocaine, Efocaine solvent, propylene glycol, and procaine hydrochloride. Eighty per cent concentrations of propylene glycol were used, except in a series of intramuscular injections at concentrations ranging from 10 to 70%. The concentrations of procaine hydrochloride tested varied from 1 to 4% aqueous solutions. Rabbits were used as test animals, except in a group of confirmatory studies in dogs and rats. The procedures for testing these agents were as follows:

1. Tests for functional and anatomical effects on peripheral nerves, by injection into the region of the sciatic nerve and the brachial plexus.

2. Tests for anatomical effects on muscle, by injection into the paravertebral muscles.

3. Tests for irritative effect on subcutaneous tissues, by the method of Kuna and Cuchie.[5]

4. Tests for irritative effect on muscle, by observation of the immediate effect of injections.

5. Studies of the mechanism of action of Efocaine, by observation of the effect on human red blood cells in vitro.

6. Localization studies, correlating the immediate distribution of injected materials with the subsequent lesions.

METHODS

The dose for all agents tested in the nerve and muscle studies in rabbits was standardized at 0.5 cc. This dose was equivalent to the minimum dosage level of 0.2 cc. per kilogram of body weight established by Carpenter and Shaffer[6] for animal tests of agents designed for the intramuscular route of administration. This level was based on the requirement of tolerance by a 50-kg. man for a 10-cc.[7] intramuscular injection. To allow for differences in animal susceptibility, these workers suggested an arbitrary safety factor of 10, thus requiring tolerance in test animals for a dose of 2 cc. per kilogram of body weight, tenfold the dose used for the studies herein reported. Comparable doses were used in the confirmatory tests in dogs (0.05 to 0.5 cc. per kilogram) and rats (0.25 to 2.5 cc. per kilogram).

All injections were made transcutaneously, according to the technique prescribed for the avoidance of pooling of the materials. A 22-gauge ¾-inch (1.9-cm.) needle was used, and injection was made slowly as the needle was withdrawn its full length. To evaluate the possibility of injury by the mechanism of pooling of a hygroscopic material, studies were made to determine the immediate distribution of all the injected substances, except procaine hydrochloride. Two procedures were used in these localization studies. In the first, a mixture of 80% propylene glycol and 20% iodopyracet (Diodrast) was injected under fluoroscopic visualization and its distribution recorded immediately thereafter on x-ray films. The second method, which is made possible by the fact that the insoluble elements in Efocaine are precipitated out as soon as it is admixed with tissue fluids, consisted of the killing and dissection of an animal directly after a series of injections. In both of these procedures, the standard injection technique was compared with a deliberate pooling method.

3. Nowill, W. K.; Hall, H. E., and Margolis, G.: An Investigation of Efocaine, a Long-Acting Local Anesthetic Agent: II. Clinical Studies, A. M. A. Arch. Surg., this issue, p. 731.

4. Hall, H. E.: Evaluation of Efocaine for Prolonged Nerve Block, read before The New York State Society of Anesthesiologists, Sixth Annual Postgraduate Assembly in Anesthesiology, Dec. 13, 1952.

5. Kuna, S., and Cuchie, F. T.: Local Irritation Caused by Streptomycin in Animals Compared to Pain Produced in Man, J. Am. Pharm. A. (Scient. Ed.) **38**:516, 1949.

6. Carpenter, C. P., and Shaffer, C. B.: A Study of Polyethylene Glycols as Vehicles for Intramuscular and Subcutaneous Injection, J. Am. Pharm. A. (Scient. Ed.) **41**:27, 1952.

7. The dose recommended for Efocaine in man is 1 to 10 cc.

The basic plan of the tests consisted of contralaterally paired injections of Efocaine and of one of the other agents into the region of the brachial plexus, along the sciatic nerve, and into the paravertebral muscles of the back. The anatomical effects of the intramuscular injections were studied at three stages, namely: the initial phase, through 6 hours; the early reactive phase, from 24 hours through two weeks, and the late regressive phase, from four weeks through 91 days. The effects of the perineural injections on nerve function were estimated by observations of the degree and duration of the motor paralysis. The initial effect was classified as partial or complete. All complete paralyses persisting 17 days or longer were classified as residual paralysis, beyond the limits of therapeutic nerve block.[8] The histologic reactions of the nerves and perineural tissues were studied in the second and third of the temporal stages listed above. A total of 80 rabbits was used. These tests are summarized in Table 1.

When the animals were killed, the sites of injection were identified, gross observations were recorded, and the tissues were removed for microscopic study. The muscles were fixed in Helly's solution, embedded in paraffin, and stained routinely with hematoxylin and eosin and occasionally with phosphotungstic acid hematoxylin. Segments of nerves were removed, along with adherent tissues, encompassing areas both proximal and distal to the region injected. Nerves were fixed in Baker's formol-calcium and embedded in paraffin, with the proximal and distal portions cut transversely and the intermediate region cut through the longitudinal

TABLE 1.—*Summary of Rabbit Tests with Efocaine, Efocaine Solvent, Propylene Glycol, and Procaine Hydrochloride (Eighty Animals)*

		Duration and Number of Studies			
Agent Tested	Site Injected	Through 6 Hr.	1-14 Days	28-91 Days	Totals
Efocaine	Muscle	23	23	23	69
	Perineural	..	28	45	73
Efocaine solvent	Muscle	9	17	23	49
	Perineural	..	28	45	73
Propylene glycol, 80%	Muscle	8	57*	..	65
	Perineural	..	23	..	23
Procaine hydrochloride, 1-4%	Muscle	..	13	7	20
	Perineural	..	12	14	26

* Includes 42 injections of graded concentrations of 10 to 70% in six rabbits.

axis. The hematoxylin-eosin stain and the Holmes silver-impregnation method for axis-cylinders were routinely employed. Selected sections were reserved for freezing and were stained by the oil red O and Sudan black B methods for fat and the Schroeder method for myelin. Some nerves were fixed in Helly's solution for connective tissue staining by the Masson method.

The confirmatory tests consisted of three intramuscular injections of Efocaine and Efocaine solvent in two dogs and three rats and five intramuscular injections of propylene glycol in one dog.

The tests for local irritant effect, following the method of Kuna and Cuchie,[5] consisted of the subcutaneous injection of 0.05 cc. of an agent into the dorsal surface of a rabbit ear and observation of the degree and type of irritation after 24 and 48 hours. With this technique the reactions to nine injections of each of the tested materials were observed in three rabbits.

An estimation of the immediate irritant effect on muscle was made by observation of the presence, duration, and intensity of fasciculations produced by the agents. These observations followed injection of each type of material, the infiltrations being made both transcutaneously and into exposed muscles. The blocking effect of 0.5 cc. of procaine hydrochloride or lidocaine (Xylocaine) hydrochloride injected one minute prior to the test injections was studied in 14 instances. The lesions resulting from these combinations of agents were observed at 30 minutes and at 24 hours and compared with those produced by the standard tests.

8. Actually, all functional changes produced by the substances containing no anesthetic agents are to be regarded as toxic effects.

The effect of Efocaine on red cells was studied by two procedures. First, defibrinated human blood was incubated at 37 C. for 30 minutes in solutions of Efocaine ranging from a 1:2 to a 1:32 dilution and observed for hemolysis after separation and resuspension in isotonic sodium chloride solution. Second, the direct effect of Efocaine on a slide suspension of red blood cells was observed microscopically after placement of a drop of this substance in contact with one border of the cover slip.

RESULTS

Muscle Studies.—Procaine hydrochloride produced a lesion in none of the rabbits. Efocaine, Efocaine solvent, and propylene glycol produced an identical necrotizing effect of severe degree. The development of this lesion was altered in no way by the previous instillation of an equivalent amount of procaine hydrochloride or of lidocaine hydrochloride, or by the addition of iodopyracet to propylene glycol. A composite description will suffice for the effects of these agents.

In muscle sectioned as early as 30 minutes following an injection, the ultimate lesion could be defined (Fig. 1*D* and *F*). Already the infiltrated area was indicated by a zone of pallor; after one hour it was more sharply demarcated by its pale coagulated appearance. This alteration, which occurred after injection of all the agents containing propylene glycol, differed from the early appearance produced by precipitation of the insoluble agents in Efocaine. Whenever this gross change was observed in the tissues, it could be predicted that all the features of necrobiosis would invariably follow. The affected areas measured 2.5 to 3 cm. in length and 1 to 2.5 cm. in width at this stage, and the necrotizing lesion did not spread during the subsequent development of the reaction (Fig. 1*C*, *E*, and *G*). Within 30 minutes early disintegration of individual muscle fibers was recognized. By two hours the characteristic microscopic features of coagulative necrosis were observed throughout this zone, and at the end of six hours this change had clearly defined the entire infiltrated area (Fig. 2*A*). During the development of this reaction, abundant fluid containing a scant granular eosinophilic material was present throughout the infiltrated zone, widely separating muscle fibers (Fig. 2*A*), but swelling or shrinkage of cells was not striking. The demarcation of the lesion was so sharp that completely dead tissue bordered on absolutely normal muscle (Fig. 2*A* and *B*); often the necrotizing change ended abruptly as a muscle fiber passed out of the infiltrated zone. The early development, the sharp margination, and the total lethal effect constituted the basic features of all lesions. The necrosis involved at once all the tissue components, leaving the affected zone devoid of living cells. Although many muscle cells disintegrated, most of them remained for several days as necrotic coagulated fibers. A scant inflammatory exudate appeared as early as six hours, but this infiltrate never became heavy and was confined to the periphery. As the inflammatory reaction and subsequent reparative processes developed, the dead tissue became a sequestered, deeply eosinophilic mass with an intensely basophilic marginal zone. Progressive granulation tissue proliferation proceeded also from the borders.

The lesions remained at their initial size for four to five days, and then began to regress as the necrotic tissue was removed and reparative processes developed. Degenerating muscle, sequestered by this reaction, was gradually removed by phagocytosis and by lytic processes. Regenerating muscle was present as early as four days. At the end of two weeks most of the dead muscle had been removed, and the lesions were considerably shrunken. During the second month muscle regeneration and fibroblastic proliferation were the most prominent features.

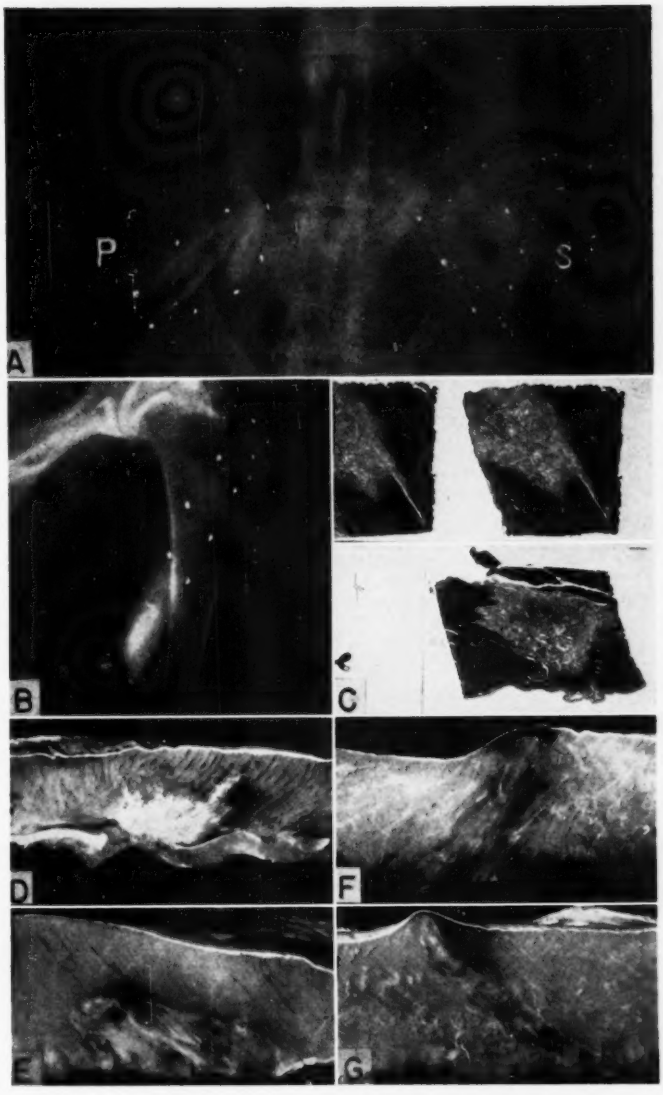

Fig. 1.—All photographs illustrate effects in rabbits of perineural or intramuscular injection of 0.5 cc. of indicated agents. *A*, x-ray taken immediately after simultaneous intramuscular injection of a mixture of 80% propylene glycol and 20% iodopyracet by pooling (*P*) and standard (*S*) techniques. × 1.

B, X-ray taken immediately after injection of same mixture into area of brachial plexus by standard technique. Heavier concentration of material is in deepest portion of injection line. × 1.

C, tissue preparation, showing lesion in muscle 24 hours following injection of Efocaine (above) and Efocaine solvent (below). Phosphotungstic acid hematoxylin stain; × 1.

D, paravertebral muscle, showing precipitate 30 minutes following injection of Efocaine. × 1.

E, lesion in muscle 24 hours after administration of Efocaine. × 1.

F, muscle 30 minutes following injection of Efocaine solvent. × 1.

G, lesion in muscle 24 hours after injection of Efocaine solvent. × 1.

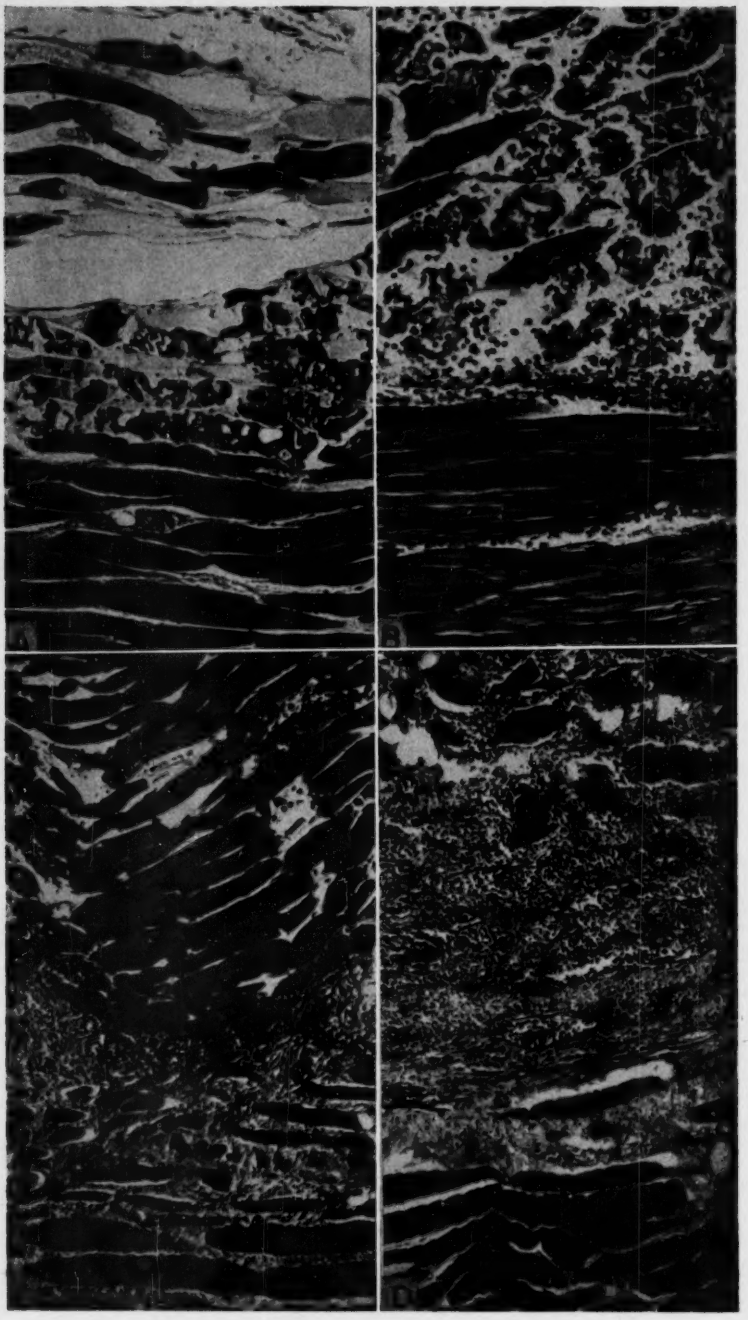

Fig. 2.—*A*, early sharply bordered necrotizing reaction in muscle six hours after administration of Efocaine. Hematoxylin-eosin stain; × 90.

B, further development of lesion 24 hours following injection of Efocaine. Hematoxylin-eosin stain; × 155.

C, sequestered necrotic muscle, bordered by zone of regenerating muscle at margin of lesion seven days following administration of 20% propylene glycol. Hematoxylin-eosin stain; × 90.

D, border of muscle lesion, showing necrotic muscle fragments, infiltration, and fibroblastic proliferation seven days following injection of 10% propylene glycol. Hematoxylin-eosin stain; × 75.

Resolution was virtually complete in lesions studied in the third month. Regenerating nerves were observed after the other reactions had disappeared and often represented the only identifying features of the lesions.

In six rabbits a series of graded concentrations of propylene glycol ranging from 10 to 70% was injected intramuscularly, and the effects were studied at the end of seven days. At all these concentrations necrotizing lesions were produced, with the following features. With the 50 to 70% concentrations, the lesions were essentially similar to those produced by 80% concentrations. With the 20 to 40% concentrations, the lesions were progressively smaller, and the zones of total necrosis were bordered by broad areas in which necrosis was incomplete and in which abundant connective tissue proliferation and muscle regeneration were proceeding (Fig 2*C*). With the 10% concentration, the necrotizing action, while severe, was incomplete, partially sparing the more resistant connective tissues (Fig. 2*D*). Injury to small intramuscular nerve fascicles was observed with all these concentrations.

Nerve Studies.—The effects of perineural injection of Efocaine, Efocaine solvent, and propylene glycol were essentially identical. Early and late observations of nerve function, tabulated for a portion of the animals, are summarized

TABLE 2.—*Summary of Functional Changes in Nerve Produced by Efocaine, Efocaine Solvent, Propylene Glycol, and Procaine Hydrochloride*

	Initial Effect			Late Effect	
Agent Tested	Observations	Partial Paralysis	Total Paralysis	Observations	Residual Paralysis
Efocaine	62	28	28	45	10
Efocaine solvent	62	42	24	45	8
Propylene glycol, 80%	12	6	6	..	..
Procaine hydrochloride, 1-4%	26	0	26	14	0

in Table 2. A total initial paralysis was produced by 50% or less of the injections of agents containing propylene glycol. The incidence of residual paralysis was approximately 20% after injection of both Efocaine and Efocaine solvent. The ratio of brachial plexus to sciatic nerve involvement was 2:1. Procaine hydrochloride, a more diffusible agent, produced a total initial nerve block in all the injections and left no residual paralysis.

The changes produced in nerve were classified according to the categories of nerve injury proposed by Sunderland.[9] This classification lists five degrees of injury, of an ascending order of severity, based upon a progression of functional and structural changes. Its essential features are as follows:

1. First-degree injury is defined as a block in conduction along axons, reversible in nature, and not accompanied with loss of continuity and Wallerian degeneration.

2. Second-degree injury denotes destruction of axons with preservation of supporting structures. The maintenance of continuity of endoneurial tubules allows precise regeneration along original pathways.

3. Third-degree injury comprises destruction of axons and disorganization of the internal structure of a nerve funiculus, in which endoneurial tube continuity

9. Sunderland, S.: A Classification of Peripheral Nerve Injuries Producing Loss of Function, Brain **74**:491, 1951.

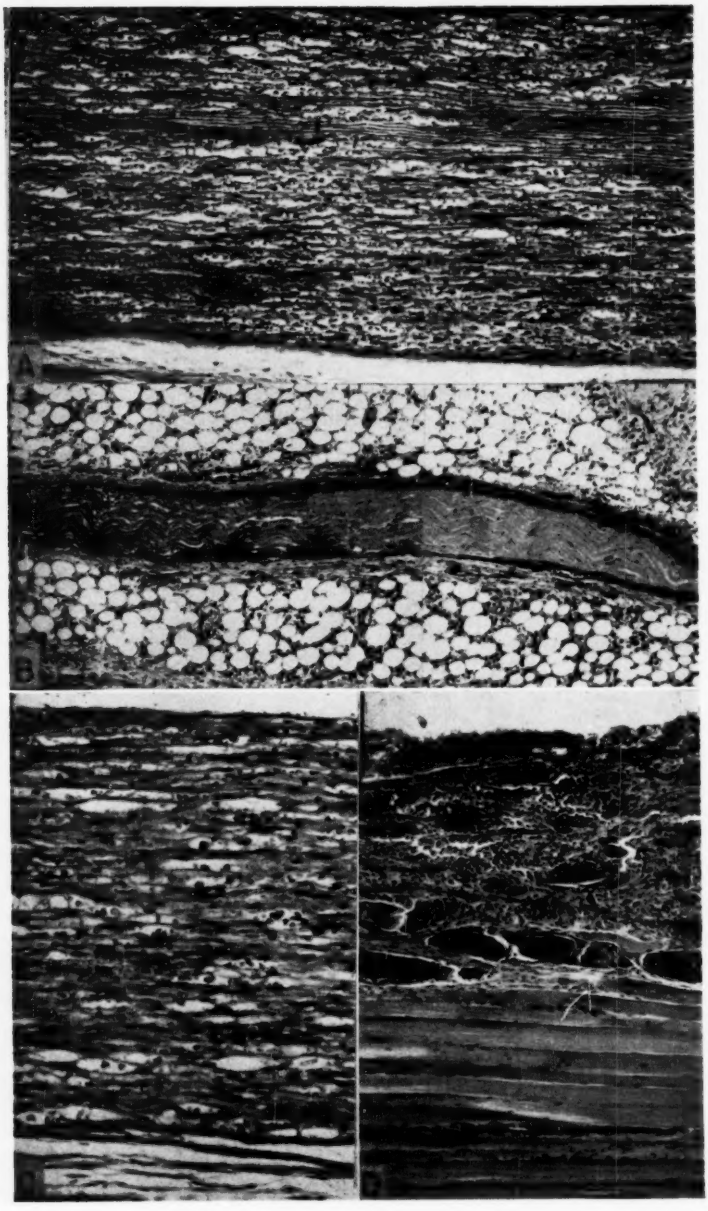

Fig. 3.—*A*, second-degree nerve injury, showing disintegration of axis-cylinders seven days after administration of Efocaine. Holmes stain; × 110.

B, fourth-degree nerve injury, showing broad zone of necrosis involving all elements in funiculus seven days after injection of Efocaine. Hematoxylin-eosin stain; × 50.

C, second-degree nerve injury, showing disintegration of myelin seven days following administration of Efocaine. Hematoxylin-eosin stain; × 130.

D, surface reaction in muscle adjacent to sciatic nerve four days following perineural injection of Efocaine. Hematoxylin-eosin stain; × 100.

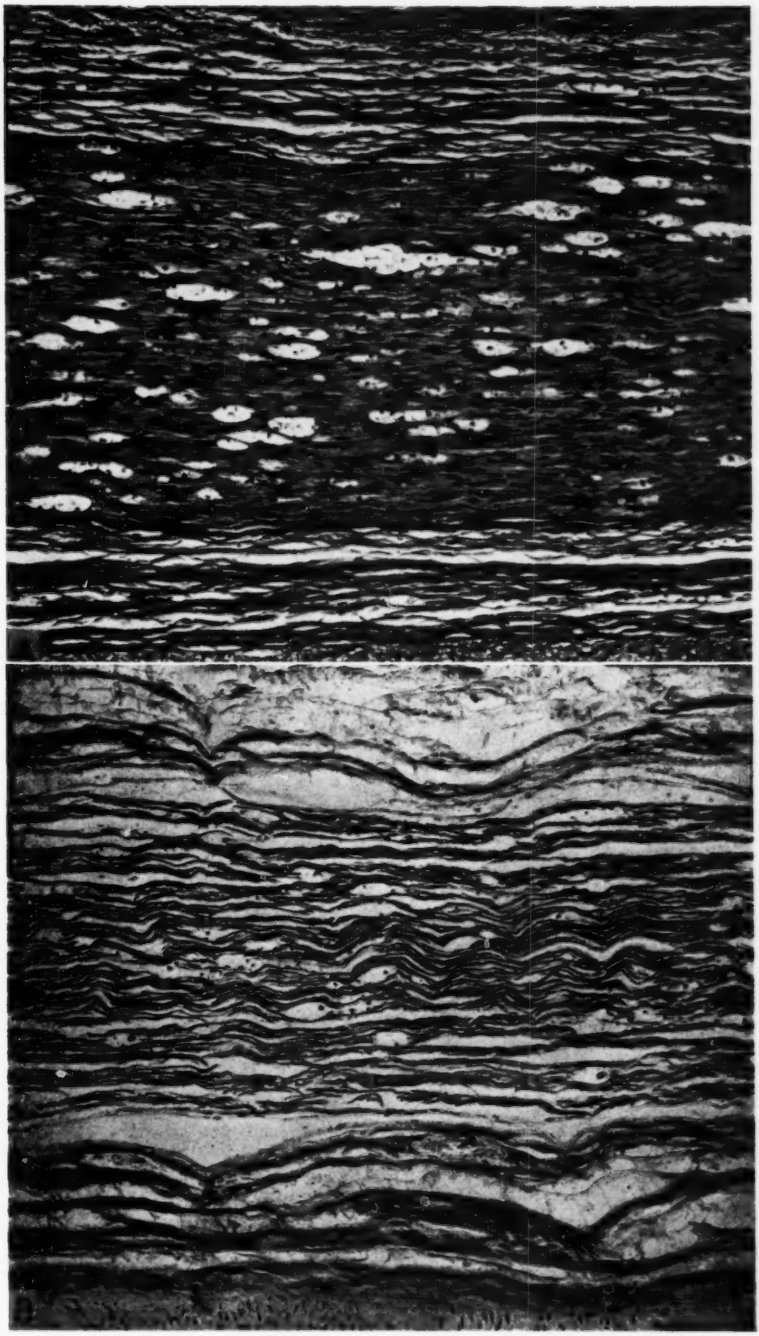

Fig. 4.—*A*, sequelae to third-degree nerve injury at 60 days following administration of Efocaine. Intrafunicular fibrosis, phagocytosis of myelin, neurilemmal and perineural proliferation. Hematoxylin-eosin stain; × 110.

B, delicate regenerated axons in same nerve. Holmes stain; × 110.

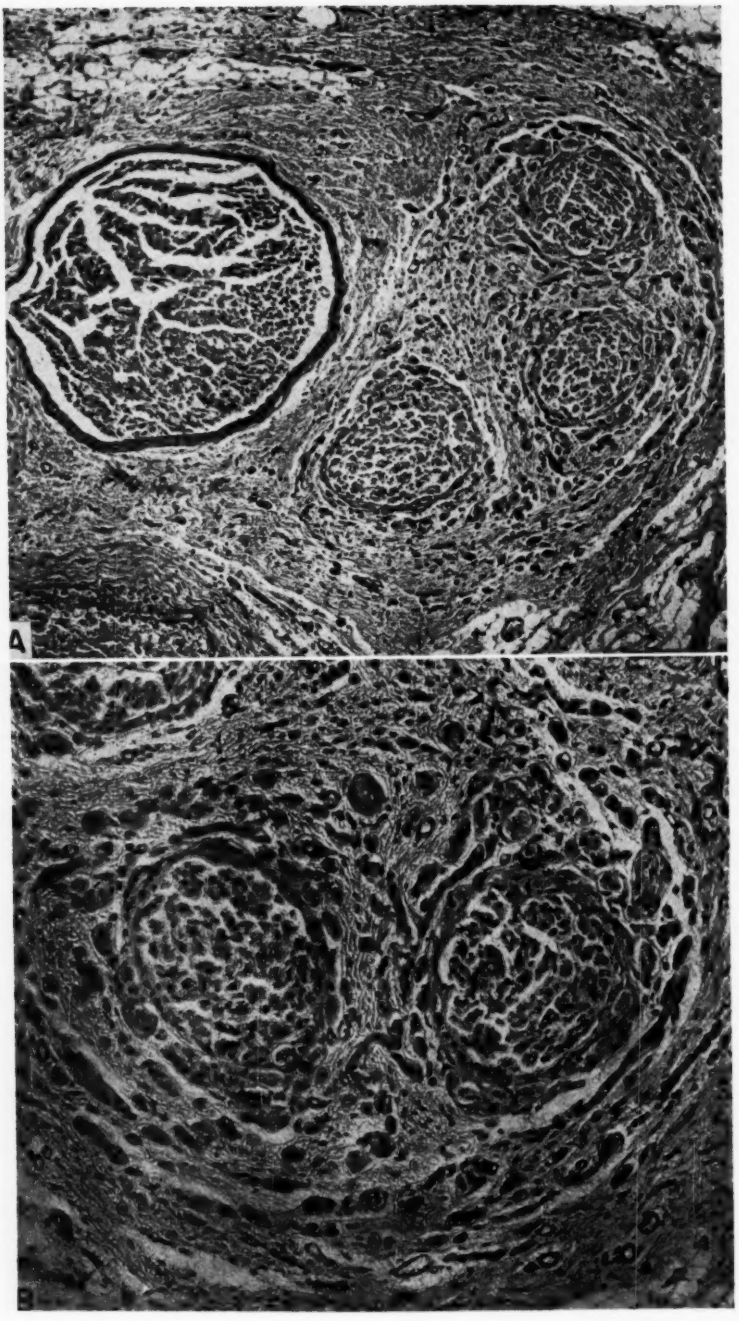

Fig. 5.—*A*, brachial nerve, showing sequelae to fourth-degree injury at 75 days after administration of Efocaine. Traumatic neuroma involving three funiculi. Holmes stain; × 85.
B, detail of two neuromatous outgrowths shown in *A*. Holmes stain; × 150.

is lost. Axonal regeneration, proceeding by chance invasion of distal tubules and often hampered by interfascicular fibrosis, produces only partial recovery of function.

4. Fourth-degree injury consists of a severe disorganization of the nerve funiculus, including the epineurium, but with preservation of the continuity of the nerve trunk. Regeneration is complicated by disorganization and fibrosis, and neuroma formation is a common feature.

5. Fifth-degree injury implies loss of continuity of the nerve trunk, with negligible recovery unless aided by nerve suture.

The classification of nerve injuries in the early groups was based upon observations of the degenerative changes. Those injuries in the late groups were classified according to the residual changes and the type of regenerative activity present. All nerves in which neuropraxia had been produced without subsequent structural change were classified as showing first-degree injury. Arbitrarily, all destructive lesions of nerve featured by myelin breakdown and axonal degeneration in the early stages (Fig. 3*A* and *C*), or by regeneration without significant intrafunicular

TABLE 3.—*Classification of Nerve Lesions Produced by Efocaine, Efocaine Solvent, Propylene Glycol, and Procaine Hydrochloride*

Degree of Nerve Injury	Efocaine	Efocaine Solvent	Propylene Glycol, 80%	Procaine Hydrochloride, 1-4%
First	30	29	11	26
Second	27	31	10	0
Third	12	12	0	0
Fourth	4	1	2	0
Fifth	0	0	0	0
Totals	73	73	23	26

fibrosis, were classified as second-degree injury, even though complete integrity of the supporting tissues was not always preserved. Nerves showing necrosis of all elements within the funiculus during the early stages or advanced intrafunicular fibrosis during regenerative phases (Fig. 4*A* and *B*) were classified as presenting third-degree injury. When extensive segments of nerve were completely necrotic during early periods (Fig. 3*B*), or when neuromatous outgrowths were observed at late stages (Fig. 5*A* and *B*), the injuries were classified as fourth degree.

The histologic lesions, classified according to these criteria, are summarized in Table 3. Destructive nerve lesions in each series numbered as follows: Efocaine, 43 of 73; Efocaine solvent, 44 of 73; propylene glycol, 12 of 23, and procaine hydrochloride, 0 of 26. The incidence of third- and fourth-degree injury was approximately 20%, a figure in agreement with the frequency of recognized residual paralysis.

The destructive lesions of nerve ranged from axonal and myelin disintegration (Fig. 3*A* and *C*) to a necrotizing effect just short of anatomical severance (Fig. 3*B*). In the early stages of the injury the severest lesion observed consisted of 5- to 6-mm. segments of necrosis affecting all elements within the perineurium of multiple funiculi. This grade of injury was observed in four nerves, in three after use of Efocaine and in one after injection of propylene glycol. There was no evidence of hemorrhage or of physical discontinuity to suggest a traumatic

injection. Neuromatous outgrowths (Fig. 5*A* and *B*), the inevitable sequelae of such lesions, were observed in three instances studied at 75 and 90 days following injury. Two of these occurred after injection of Efocaine, the other after administration of Efocaine solvent.

Reactions in the perineural tissues were constantly observed during the second stage. An initial inflammatory exudate of moderate intensity was accompanied with focal necrotizing changes in adipose tissue. Necrotizing lesions of vessels were present in 16 specimens, accompanied with thrombosis (Fig. 6*A*) in 5. The intensity of this reaction often bore no relation to the degree of nerve injury, however. Subsequently, progressive proliferation of granulation tissue produced dense fibrous scars (Fig. 6*B*) that were grossly demonstrable. Foreign-body reactions, presumably secondary to extensive fat necrosis, were present in two specimens examined as late as 60 days following the injections and in one specimen after 75 days. Generally, however, perineural fibrosis was not prominent in the late stages.

Subcutaneous Tissue Irritation.—The sites of subcutaneous injection of 0.05 cc. of these agents remained as slightly elevated pale zones for approximately five minutes, then disappeared. At the end of 24 and 48 hours the areas of procaine hydrochloride injection were not grossly recognizable. Where the other agents had been injected, 0.3- to 0.5-cm. foci of necrosis developed, and many of these became ulcerated. By the criteria of Kuna and Cuchie,[5] these lesions were graded as of maximum severity.

Muscle Irritation.—Immediately after infiltration of standard 0.5-cc. doses of Efocaine, Efocaine solvent, and propylene glycol, strenuous muscle fasciculations were observed, originating at the injection site and spreading over the muscle for approximately 5 cm. These abnormal contractions lasted about one and a half minutes following Efocaine injection and about four and a half minutes after administration of the other materials. When injections were made into exposed muscle, as little as 0.01 cc. was observed to produce fasciculations. This reaction was prevented by previous injection of procaine hydrochloride or of lidocaine hydrochloride. When this reaction subsided, the injected area was no longer responsive to mechanical stimuli, whether or not anesthetic agents had been used. This loss of irritability, correlated with the coagulated appearance of the muscle within 30 minutes after injections and the subsequent fate of the infiltrated muscle, was interpreted as the result of an extremely rapid noxious action, rather than as evidence of a short-acting irritant effect.

Confirmatory Tests.—These tests were designed to determine whether doses of Efocaine, Efocaine solvent, or propylene glycol at levels in the range administered to rabbits would have a necrotizing effect in dogs and rats. Necrosis of muscle comparable with the lesions in rabbits was consistently observed after 11 injections. These findings indicate that an unusual susceptibility to these substances is not a factor in the reactions produced in rabbits.

In Vitro Studies.—Complete hemolysis was produced by Efocaine at dilutions of 1:8 or less. The remarkable hygroscopic activity of Efocaine was demonstrated by the slide-suspension studies. Immediately after placement of the Efocaine droplet, the red cells were rapidly swept toward the agent on the current generated by the absorption of fluid. This extraction of the aqueous medium continued until the red cells were agglutinated into an amorphous mass.

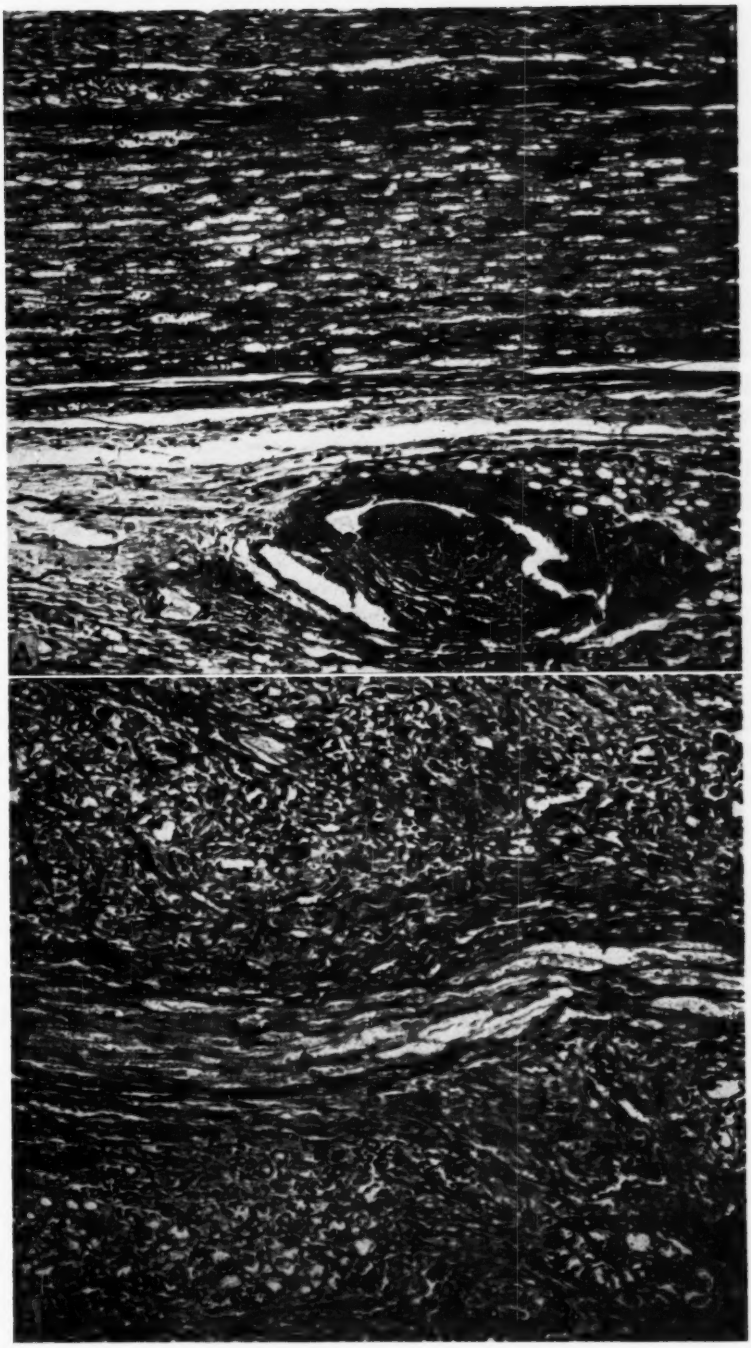

Fig. 6.—*A*, venous thrombus in perineural connective tissue nine days after injection of Efocaine solvent. Hematoxylin-eosin stain; × 90.

B, proliferating perineural granulation tissue nine days following administration of Efocaine solvent. Hematoxylin-eosin stain; × 72.

Localization Studies.—The x-ray studies of the immediate localization of the propylene glycol-iodopyracet compound demonstrated a linear distribution with the standard technique, contrasting with the focal deposits produced by deliberately pooled injections (Fig. 1*A* and *B*). The rapid precipitation of the insoluble agents in Efocaine made it possible to identify the site of immediate infiltration of muscle almost as quickly as an animal could be given the injection, killed, and dissected (Fig. 1*D*). In animals dissected under direct visualization, the infiltrated area was defined within one or two minutes as a yellow opaque zone. In the case of propylene glycol or Efocaine solvent, the extent of the infiltrated tissue was demarcated within 30 minutes (Fig. 1*F*).

With the use of these two procedures, a direct comparison was made of the immediate intramuscular localization of the injection, the earliest gross changes, and the fully developed lesion. There was an identity in the size of the infiltrated zone and of the early and the full-blown lesions, indicating that the primary localization of the injected material determined the size and distribution of the subsequent lesion. A pooling technique influenced the action of the agent only by determining the area immediately infiltrated.

Dissection of the sites of perineural injection at the initial stage and during the first four to five days following injections demonstrated that the transcutaneous, nonpooling technique did not result in precise perineural deposition of the agents. Widely scattered foci of necrosis within and along the surfaces of adjacent muscle (Fig. 3*D*) indicated that in many instances only a fraction of the material had been placed perineurally. X-rays also demonstrated a varying concentration of the administered material along the line of injection (Fig. 1*B*). These observations explained differences in the functional effects and the wide variations in the degree of nerve injury, which contrasted so sharply with the uniform severity of the muscle lesion.

COMMENT

There is adequate experimental background to indicate that, despite its hygroscopic properties, propylene glycol has a low systemic toxicity.[10] However, animal tests of its acceptability as an agent for focal parenteral injection have yielded results that may be questioned. McGavack and Vogel[11] noted tissue injury and inflammatory reaction secondary to repeated intramuscular injections of 1-cc. doses in dogs but did not consider the reaction of significance. Carpenter and Shaffer[6] produced necrosis in rats by intramuscular injections of doses of 0.4 to 2 cc. per kilogram of body weight, but considered this effect as an "ischemic necrosis" produced when "the compound was forced into the muscle bundle." Weinberg,[12]

10. Seidenfield, M. A., and Hanzlik, P. J.: The General Properties, Actions and Toxicity of Propylene Glycol, J. Pharmacol. & Exper. Therap. **44**:109, 1932. Hanzlik, P. J.; Newman, H. W.; Von Winkle, W., Jr.; Lehman, A. J., and Kennedy, N. K.: Toxicity, Fate, and Excretion of Propylene Glycol and Some Other Glycols, ibid. **67**:101, 1939. Morris, H. J.; Nelson, A. A., and Calvery, H. O.: Observations on the Chronic Toxicities of Propylene Glycol, Ethylene Glycol, Diethylene Glycol, Ethylene Glycol Mono-Ethyl-Ether, and Diethylene Glycol Mono-Ethyl-Ether, ibid. **74**:266, 1942.

11. McGavack, T. H., and Vogel, M.: Propylene Glycol as a Menstruum for the Administration of the Steroid Hormones, J. Lab. & Clin. Med. **29**:1256, 1944.

12. Weinberg, T.: A Study of the Effects of Efocaine upon Nerves, Muscle, Skin and Subcutaneous Tissue, Sinai Hosp. J. **1**:21, 1952.

studying the effects of Efocaine in rabbits, encountered necrotizing changes in muscle and fat, degenerative changes in nerves, fibroblastic proliferation, and bland thrombi after 0.5-cc. doses. These lesions were likewise considered to be of mechanical origin, and it was concluded that this was "a benign process which is apparently reversible." However evaluated, it is apparent that tissue damage was a constant observation in these studies. It is evident, then, that at least part of the discrepancy between our studies and those in the literature may reside not in the results but in the interpretations given to them. Our tests demonstrate that Efocaine has a severe necrotizing effect on animal tissue at doses within the levels used therapeutically in man.

Our observations at the late stages of the study could possibly be used to support the interpretation that the reaction to Efocaine is a reversible one, since some of the nerve lesions, and all those in muscle, eventually regress. The remarkable healing of the severe muscle lesions indicates how deep-seated soft tissue lesions in man can disappear completely, so that a noxious effect may never be observed. Therefore, it is understandable how propylene glycol has gained the reputation of being an innocuous agent. However, with the introduction of Efocaine a new situation is presented. For the first time a pharmaceutical preparation consisting largely of propylene glycol has been compounded with the target being nerve. Obviously, the concept of "benign necrosis" loses all validity when applied to the nervous system.

Parallel examples are furnished by the antibiotics penicillin and streptomycin, which rarely produce clinically detectable lesions in man unless accidentally deposited within or adjacent to a nerve.[13] That penicillin will produce necrosis of nerve and muscle is not recognized widely enough. The occurrence of necrosis of the lumbosacral spinal cord of a rabbit observed by Tarlov and associates[13b] after injection of 0.07 cc. of penicillin into the epineurial sheath of each sciatic nerve serves as a further warning of the danger inherent in the introduction of destructive agents in relation to nerves close to the spinal axis.

Propylene glycol, the solvent vehicle which comprises 78% of Efocaine, duplicates all the effects of the complete drug and is considered to be the noxious agent.[14] In view of the lack of systemic toxicity of propylene glycol,[10] it is probable that the effect is entirely the result of the hygroscopic action of this substance. Propylene glycol may exert its effect by extracting water from cells, by absorbing extracellular and intravascular fluids, or possibly by entering cells and carrying fluids along. The rapidity of onset of the lesions, the sharpness of demarcation, and the total necrosis produced eliminate the possibility that the effect is a simple mechanical one or an ischemic necrosis secondary to massive imbibition of fluid by a hygroscopic agent pooled within a confined space. If the action of propylene glycol is

13. (*a*) Holbrook, T. J., and Pilcher, C.: The Effects of Injection of Penicillin, Peanut Oil and Beeswax, Separately and in Combination upon Nerve and Muscle; An Experimental Study, Surg., Gynec. & Obst. **90**:39, 1950. (*b*) Tarlov, I. M.; Perlmutter, I., and Berman, A. J.: Paralysis Caused by Penicillin Injection: Mechanism of Complication—A Warning, J. Neuropath. & Exper. Neurol. **10**:158, 1951. (*c*) Woodhall, B.; Broadbent, T. R., and Javer, J.: Neuropathology of Antibiotic-Induced Peripheral Nerve Paralysis, S. Forum (1950), p. 394, 1951.

14. The possibility of an additive effect by butyl-*p*-aminobenzoate, procaine base, or polyethylene glycol 300 has not been ruled out by animal tests.

through its hygroscopic effect, a striking difference in cell permeability or in the constitution of intercellular tissues would be required before a material variation in species susceptibility could be expected.

The continued use of Efocaine in man for any other purpose than to destroy nerve would be dependent upon the demonstration of a nontoxic therapeutically effective dose of this agent. Basically, this would require elimination of the destructive action of the propylene glycol contained in the solvent. The disparity between the concentration of this material in Efocaine (78%) and its minimum toxic concentration (less than 10%) indicates the dilution factor needed to achieve this effect. The constitution of the preparation eliminates the possibility of dilution in vitro. Even a wet syringe initiates precipitation of the water-insoluble anesthetic agents. Nor does it appear possible, at least in the rabbit, to approach this problem by the alternative method of reduction of the size of the dose. An amount as small as 0.05 cc. still retains a necrotizing action.

The problem of establishing the theoretical basis for the new anesthetic principle advanced for Efocaine still remains. The propylene glycol content in the solvent has been demonstrated to produce in animals all the effects of the complete drug, including paralysis of nerve function, as well as destructive lesions. Manifestly, it is not possible to test for a first-degree injury in the presence of a more advanced lesion.

SUMMARY

A severe destructive effect of Efocaine on rabbit tissues was demonstrated with 0.5-cc. doses, equivalent to 10-cc. doses in man. The major noxious substance in Efocaine is propylene glycol, which comprises 78% of the solvent vehicle for Efocaine. This material retains a destructive effect in 0.5-cc. doses, even when diluted as much as 1:8. Reduction of the dose level of Efocaine to 0.05 cc. does not eliminate the necrotizing effect of this substance. This necrotizing action was confirmed by tests in dogs and rats.[15] In the face of the functional and structural effects on nerve produced by the solvent vehicle for Efocaine and by propylene glycol alone, the part the precipitated anesthetic agents in this drug play in the production of prolonged anesthesia is impossible to determine.

15. Subsequent to the submission of this manuscript the effects of Efocaine solvent were studied in one monkey, killed one week after the following series of injections: right brachial plexus, 0.25 cc. of Efocaine transcutaneously; left brachial plexus, 0.25 cc. of Efocaine solvent transcutaneously; right sciatic nerve, 0.1 cc. of Efocaine solvent intraneurally; left sciatic nerve, 0.05 cc. of Efocaine solvent intraneurally; right paravertebral muscle, 0.1 cc. Efocaine, and left paravertebral muscle, 0.1 cc. Efocaine solvent. Third and fourth degree injury was observed in all the nerves studied, except for the left brachial plexus. The latter had no anatomic lesions in the nerves, but presented an intense reaction in the neighboring muscle and connective tissues. Necrotizing lesions comparable to those seen in the other animals were produced at the sites of intramuscular injection.

AN INVESTIGATION OF EFOCAINE, A LONG-ACTING LOCAL ANESTHETIC AGENT

II. Clinical Studies

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AND
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DURHAM, N. C.

IN THE preceding paper,[1] a description is given of the chemical nature and theoretical mode of action of Efocaine. The anatomical effects of this material on animal tissues are described in detail. This paper reports concurrent clinical studies.

Since its introduction, Efocaine has been used by numerous anesthetists and surgeons with apparent satisfactory results. The use of this agent in anorectal and perineal surgery was reported by Tucker,[2] Gross and Shaftel,[3] and Cappe and Pallin.[4] These authors concluded that Efocaine is a safe and effective agent for control of postoperative pain. This drug has been advocated for inducing intercostal blocks to control pain and prevent pulmonary complications in patients having thoracic and upper abdominal surgery. After clinical trial, Deaton and Bradshaw,[5] Deaton,[6] and Puderback and Shaftel [7] recommended its use. Iason and Shaftel,[8] Bartlett and Eastwood,[9] and Roualle [10] reported results of its use in various

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1. Margolis, G.; Hall, H. E., and Nowill, W. K.: An Investigation of Efocaine, A Long-Acting Local Anesthetic Agent: I. Animal Studies, A. M. A. Arch. Surg., in publication.

2. Tucker, C. C.: The Control of Postoperative Pain in Ano-Rectal Surgery, J. Kansas M. Soc. **53**:230-234, 1952.

3. Gross, J. M., and Shaftel, H. E.: The Role of Efocaine in Ano-Rectal Anesthesia and Analgesia, New York J. Med. **52**:1413-1417, 1952.

4. Cappe, B. E., and Pallin, I. M.: Prolonged Relief of Post Episiotomy Pain, Am. Pract. & Digest. Treatment **3**:739-741, 1952.

5. Deaton, W. R., Jr., and Bradshaw, H. H.: A Long-Lasting Local Anesthetic: Use in Thoracic Surgery, Am. Surgeon **18**:616-620, 1952.

6. Deaton, W. R., Jr.: The Use of a New Long-Lasting Local Anesthetic Solution for the Relief of Pain After Thoracoplasty and Pulmonary Resection, Am. Surgeon **19**:349-353, April, 1953.

7. Puderback, W. J., and Shaftel, H. E.: Prolonged Intercostal Nerve Block in Upper Abdominal Surgery, Journal-Lancet **72**:200-204, 1952.

8. Iason, A. H., and Shaftel, H. E.: A New Approach to the Problem of Postoperative Pain, Am. J. Surg. **83**:549-555, 1952.

9. Bartlett, R. W., and Eastwood, D. W.: Long-Acting Intercostal Nerve Block for Upper Abdominal Surgery, Surgery **32**:956-960, 1952.

10. Roualle, H. L. M.: Prolonged Wound Analgesia After Surgical Operation: Clinical Trial of Efocaine, Brit. M. J. **2**:1293-1295, 1952.

surgical incisions by techniques ranging from local injection to intercostal blocks. They saw no evidence of interference with wound healing or of the adverse tissue reactions that have been reported after the use of oil-base substances.

One hundred patients having thoracic surgery were studied (Table 1). In 50 of these, the intercostal nerves were injected under direct vision by the surgeon before the incision was closed. The technique utilized was injection of 2 or 3 cc. of the agent into the two nerves above and the two below the incision. Neither surgeon nor anesthetist knew which solution was being injected: Efocaine or Efocaine solvent. The remaining 50 patients received no injection and were used as controls. These 100 patients were followed in the postoperative period particularly with reference to amount of narcotics administered and severity of pain. Neither

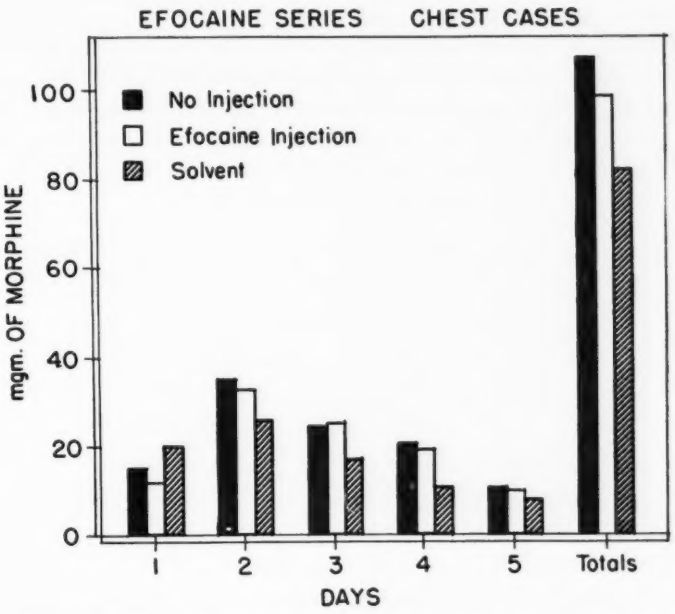
TABLE 1.—*Types of Thoracic Surgery in 100 Patients in Experimental and Control Series*

	Efocaine or Efocaine Solvent	Control	Total
Thoracotomies			
Partial esophagectomy	5	2	7
Lobectomies, etc. (tuberculosis)	23	13	36
Removal of carcinoma of lung	8	10	18
Mitral valvotomy	..	2	2
Treatment of bronchiectasis	1	..	1
Repair of patent ductus arteriosus	1	1	2
Repair of ruptured diaphragm	1	1	2
Removal of intrathoracic goiter	1	..	1
Wrapping of thoracic aneurysm	..	1	1
Removal of lung cyst	..	1	1
Repair of coarctation of aorta	..	1	1
Thoracoplasties	10	18	28
Totals	50	50	100

patient nor ward nurse was aware that this nerve-blocking procedure had been done. These methods were aimed at keeping the interpretation of the degree of postoperative pain as objective as possible.

Narcotics administered on the day of operation and for four days thereafter were tabulated, and the mean dosage was obtained for both series. Morphine requirements, per patient, were as follows: control series, 107 mg.; Efocaine series, 98.5 mg., and Efocaine solvent series, 82 mg. (Figure). By statistical analysis these differences in dosage were not significant. However, much of the administration of narcotics appeared to be for relief of symptoms unrelated to the operative incision. Pain in the shoulders, bladder distention, apprehension, and restlessness were other causes for administration of narcotics. Patients with multiple procedures were included in both series, and their reactions with and without injection of the anesthetic agent were compared. Clinical effects and narcotic requirements of five thoracoplasty patients are summarized in Table 2. It was noted that these patients subjectively experienced less pain when treated with Efocaine, but the morphine requirements were variable. During these five days of observation, the clinical impression was gained that patients of the treated series appeared to have somewhat less pain in the operative site than those of the control series (Table 3).

Three patients with intercostal injection experienced severe chest pain beginning on the fifth and sixth postoperative days. Whether this was related to the surgical trauma itself or to the Efocaine effect is debatable. However, such pain was not observed in the control group. One patient continued to have severe chest pain



Postoperative morphine requirements of patients with thoracic surgery; comparison of 50 in experimental series with 50 in control series.

TABLE 2.—*Clinical Effects and Narcotic Requirements of Five Thoracoplasty Patients*

Name; Age, Yr.; Race; Sex	Efocaine Administered	Efocaine Not Administered	Morphine, Mg.*	Patient's Statement
C. K.; 20;	1st stage	.....	100	"Soreness"
W; M	2d stage	.....	70	"Soreness"
	.....	3d stage	75	"Pain worse this time than others"
P. C.; 28;	.....	1st stage	130	"Terrible pain"
W; M	2d stage	.....	137.5	"Pain less than last time"
	.....	3d stage	250	"Pain pretty bad"
C. C.; 35;	.....	1st stage	190	"Hurt pretty bad"
W; M	.....	2d stage	200	"Bad pain"
	3d stage	.....	100	"Soreness, more pain after last operation"
A. T.; 32;	1st stage	.....	110	"No definite pain, just soreness"
W; M	2d stage	.....	127	"Soreness, some pain on 6th day"
	.....	3d stage	277.5	"Hurts much more than before"
A. M.; 32; W; F	1st stage	.....	185	"Sore where they cut me—can take deep breaths fairly easily"
	.....	2d stage	120	"Pain worse than last operation"
	3d stage	.....	200	"Pain not too bad, nausea and vomiting"

* Total morphine administered in five days after operation.

after leaving the hospital and became addicted to narcotics. Although patients of the experimental series appeared to be better able to cough, breathe, and move than those of the control group, comparison of the incidence of postoperative atelectasis revealed no essential difference between the two series (three in the Efocaine series and three in the control series had atelectasis). Interference with wound healing was not noted in any of the patients.

In addition to the patients with surgery of the chest, certain patients were carefully selected for therapeutic nerve blocks with Efocaine (Table 4). These injections were uniformly effective in the production of anesthesia. The amount of solution injected in each area varied from 3 to 10 cc. Injections were made in a linear or fan-shaped manner in an effort to prevent any pooling of the material. However, complications related to the regional anesthesia did occur.

TABLE 3.—*Typical Statements of Thoracic Surgery Patients After Operation*

Control	Efocaine or Efocaine Solvent
1. "Terrible pain in my chest when I moved"	1. "No bad pain—just tightness in my chest"
2. "More pain than I expected"	2. "Not bad pain at all"
3. "No sharp pain; I feel as if a mule kicked me in the chest"	3. "No pain in my chest at all"
4. "Pain with every breath"	4. "Not a bad pain—just soreness"
5. "Sharp pain when I coughed and moved"	5. "Pain didn't bother me much"

REPORT OF CASES

Since other investigators have not reported, in the medical literature, complications related to the use of this solution, we will describe these as noted by us in detail.

CASE 1.—Mrs. R. K., aged 69, was admitted to the hospital on July 6, 1952, complaining of severe pain in left ankle and toes. Examination revealed an indolent ulcer of the left medial malleolar area, and early gangrene was manifested by pallor, cyanosis, and coldness of the second, third, and fourth toes. The diagnosis was vascular insufficiency in the left leg.

Intermittent venous occlusion, postural changes, and use of vasodilator drugs were ineffective in increasing blood flow in the extremity. On July 5 sympathetic ganglion block of the first to the third lumbar segments on the left with 1% lidocaine (Xylocaine) and Efocaine (3 cc. of each solution in each area) caused a temporary increase in temperature of the leg but produced no change in the status of the ulcer or of the toes. Pain in the foot remained severe.

A left sciatic nerve block with 2% lidocaine produced relief of pain and definitely increased vascularity of the toes for six hours. A sciatic block with 5 cc. of 2% lidocaine and 5 cc. of Efocaine later the same day produced sensory anesthesia of the extremity lasting five days. The anesthesia then gradually disappeared over the following five to seven days. During this time, gradually increasing pain was noted in the left buttock, the pain radiated over the distribution of the sciatic nerve to the foot. This discomfort was severe, requiring administration of narcotics intermittently for about two months. Pain persisted for five months before disappearing entirely.

CASE 2.—J. R., a 46-year-old Negro man, was admitted to the hospital with a diagnosis of thrombosis of posterior inferior cerebellar artery. Associated with his other symptoms, he had

severe singultus which did not respond to carbon dioxide inhalation or administration of compound spirit of ether (Hoffmann's anodyne). After four days of these symptoms, the patient was exhausted. Sedatives produced only temporary relief. Under fluoroscopic observation, the left diaphragm was noted to be contracting spasmodically. Therefore, the left phrenic nerve was injected with 3 cc. of 1% lidocaine and 5 cc. of Efocaine. Singultus stopped, but after 20 minutes

TABLE 4.—*Patients with Regional Anesthesia Induced with Efocaine or Efocaine Solvent*

Type of Injection	Diagnosis	Solution	Results
Local	Neuroma, dorsum of foot	Efocaine	Thrombophlebitis, lower part of leg, 3 days
Local	Arthritis, knee joint	Efocaine solvent	Good relief "several days"
Local	Arthritis, right hip	Efocaine solvent	Free of pain 4 wk.
Local	Trochanteric bursitis	Efocaine solvent	Relief of pain
Local	Hemorrhoidectomy	Efocaine	Minimal pain until pack removed
Local	Hemorrhoidectomy	Efocaine	Moderate pain until pack removed, then minimal pain
Local	Hemorrhoidectomy	Efocaine	Perianal inflammation, subsided
Intercostal	Recurrent carcinoma of breast	Lidocaine; efocaine	Breathed better but still some pain
Intercostal	Tracheal graft	Lidocaine; efocaine	Relief 4 days
Intercostal	Fractured ribs (9 and 10)	Lidocaine; efocaine	Relief of pain 2 days
Intercostal	Fractured rib	Lidocaine; efocaine	Relief of pain 48 hr.
Brachial block	Terminal carcinoma of lung; pain, left arm	Lidocaine; efocaine	Relief of pain 7 days
Stellate	Vasospasm	Efocaine	Relief of spasm
Stellate	Pain, left arm	Lidocaine; efocaine	Relief 5-6 hr., then severe pain 12 hr.
Stellate	Same patient	Lidocaine; efocaine	Pain in shoulder 5 hr. after injection
Stellate	Same patient	Lidocaine; efocaine	Hand almost normal, complete relief of pain
Sciatic	Vascular insufficiency, left leg	Lidocaine; efocaine	Relief 5 days
Sciatic	Embolism, right leg	Procaine; efocaine	Complete relief
Sciatic	Vascular insufficiency, right foot	Efocaine	Complete relief, postinjection sciatic neuritis 5 mo.
Sciatic	Vascular insufficiency, left leg	Efocaine	Minimal relief
Lumbar sympathectomy	Thrombophlebitis	Lidocaine; efocaine	Return of pain 1 mo. later
Lumbar sympathectomy	Vascular insufficiency, right leg	Efocaine solvent	Relief 2 days
Left phrenic block	Intractable hiccups	Efocaine	Paralysis of left diaphragm observed by fluoroscopy 9 mo.
Local	Neuroma, dorsum of foot	Efocaine solvent	Relief 4 hr.

it returned. Repeat fluoroscopy revealed paralysis of the left diaphragm, with spasmodic contractions of the right diaphragm. Follow-up fluoroscopic examinations have revealed paralysis of the left diaphragm for nine months following the original injection.

Two patients showed transient complications. One complained of severe shoulder pain of 12 hours' duration following a stellate ganglion block. The other had thrombophlebitis of the lower part of the leg after local injection of a painful scar.

In addition to these cases in our own series, one patient was referred to members of the Duke Hospital staff for consultation after complications had been produced by regional anesthesia with Efocaine.

CASE 3.—M. B. was a 34-year-old Negro man, with a history of pain in the left shoulder, for which he received an injection into the left suprascapular nerve. Within 24 hours, the patient noted marked swelling in the injected area, with extreme pain of the entire shoulder region. This pain was so severe that he required admission to the local hospital. Treatment consisted of application of heat to the shoulder area and frequent injections of meperidine (Demerol) hydrochloride. Swelling and pain gradually subsided over 10 days, but there was residual paralysis of the external rotator muscles of the shoulder (supraspinatus, infraspinatus, and rhomboid muscles).

COMMENT

The relief of pain for prolonged periods was the admirable goal in the development of the new drug, Efocaine. An analysis of the safety and effectiveness of this agent was attempted in this study. The results of the clinical tests seemed encouraging at the onset. Nerve blocks were uniformly successful in the production of anesthesia of long duration, and there appeared to be less postoperative pain in the patients with thoracic surgery. However, this impression did not stand up under statistical analysis, testimony of the difficulties inherent in the evaluation of the subjective observations of patients.[11] Postoperative narcotic requirements were not reduced by intercostal blocks with Efocaine, and there was no significant decrease of postoperative pulmonary complications. As in the animal studies, the effect of Efocaine could not be differentiated from the effect of Efocaine solvent, a finding rendering the mode of action of the complete drug open to considerable doubt. Furthermore, the use of this drug was associated with complications indicating an injurious effect. Severe intercostal neuritis occurred in three patients who had thoracic surgery, and a variety of unfavorable reactions appeared when this agent was used for other types of regional anesthesia. Inflammatory reaction to the material was seen in the example of cellulitis of the shoulder. Severe nerve injury was illustrated both by the sciatic and suprascapular neuritides and by the prolonged phrenic paralysis.

It may be argued that the complications encountered in the clinical investigation were due to trauma, infection, other local anesthetic agents, or progression of the disease. On the basis of our animal tests, these complications could have been readily predictable. The animal studies clearly demonstrated the potential necrotizing action of this drug on any tissue exposed to the undiluted material for a critical period. In these experiments it was apparent that the degree of nerve injury was correlated with the chance distribution of the material in relation to nerve tissue. Similar considerations may be used to explain the variability of nerve injury in man.

Efocaine has been introduced as a depot anesthetic solution to replace the shorter-acting preparations now available to the physician. It has been offered as an agent designed solely for the purpose of blocking nerve, without an awareness of its potential necrotizing effect. In the future the physician considering the therapeutic use of this drug should be protected by the knowledge that in its action the material is comparable with alcohol rather than with procaine. As soon as this destructive action was demonstrated by us, the clinical use of Efocaine was discontinued at Duke Hospital.

11. Papper, E. M.; Brodie, B. B., and Rovenstine, E. A.: Postoperative Pain: Its Use in the Comparative Evaluation of Analgesics, Surgery **32**:107-109, 1952.

SUMMARY

The prolonged anesthetic effect of Efocaine was verified by clinical studies. Although subjective relief of pain was noted with the use of Efocaine, a significant decrease in postoperative complications and in requirements for narcotics was not observed. Since anesthesia could also be produced by the Efocaine solvent (78% propylene glycol and 2% polyethylene glycol 300), which contains none of the anesthetic agents, the mode of action of this drug is questioned. Complications, namely, neuritis, inflammatory reactions, and lasting absence of nerve function, resulted from the clinical use of this drug.

CONCLUSION

Efocaine does not fulfill the requirement for a local anesthetic agent producing anesthesia of long duration without toxic effect.

NEUROLOGICAL COMPLICATIONS FOLLOWING THE USE OF EFOCAINE

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AND
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MANY FAVORABLE reports on the use of Efocaine [1] as a long-acting local anesthetic drug have been published in the past two years.[2] Studies of histological changes following the injection of this drug in various animals have been reported previously by us.[3] These changes may be summarized as follows: necrosis of muscle followed by regeneration and connective tissue proliferation; nerve destruction of varying degrees of severity, the repair of which may be associated with neuroma formation. It is not unexpected, therefore, to see reports of complications associated with the use of this drug appear in the medical literature. Bonica [4] noted 6 cases of postinjection neuritis in 100 cases in which this drug was used. Eastwood and Bartlett [5] recently stated that they have discontinued the clinical use of Efocaine because of similar complications. Shapiro and Norman [6] reported three serious complications following the injection of this drug, namely, transverse myelitis with paraplegia secondary to intercostal nerve block; lumbosacral nerve involvement following paracervical injection in a woman during labor, resulting in severe disabling symptoms in the left leg; and prolonged interruption of sympathetic function following intercostal nerve block.

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1. Efocaine is a trade name of E. Fougera & Co., New York.

2. Puderbach, W. J., and Shaftel, H. E.: Prolonged Intercostal Nerve Block in Upper Abdominal Surgery, Journal-Lancet **72**:200 (April) 1952. Iason, A. H., and Shaftel, H. E.: A New Approach to the Problem of Postoperative Pain, Am. J. Surg. **83**:549, (April) 1952. Iason, A. H., and Shaftel, H. E.: A New Approach to the Problem of Postoperative Pain, Am. J. Surg. **83**:549 (April) 1952. Gross, J. M., and Shaftel, H. E.: The Role of Efocaine in Anorectal Anesthesia and Analgesia, New York J. Med. **52**:11, 1413 (June 1) 1952. Deaton, W. R., Jr., and Bradshaw, H. H.: Relief of Post-Thoracotomy Pain, Surg., Gynec & Obst. **97**:140 (Aug.) 1953.

3. Margolis, G.; Hall, H., and Nowill, W. K.: An Investigation of Efocaine, A Long-Acting Local Anesthetic Agent: I. Animal Studies, this issue, p. 715.

4. Bonica, J. J.: Management of Intractable Pain with Analgesic Blocks, J. A. M. A. **150**: 1581 (Dec. 20) 1952.

5. Eastwood, D. W., and Bartlett, R. W.: Efocaine, Correspondence, J. A. M. A. **152**:1067 (July 11) 1953.

6. Shapiro, S. K., and Norman, D. D.: Neurological Complications Following the Use of "Efocaine": Report of 3 Cases, J. A. M. A. **152**:608 (June 13) 1953.

Three cases of severe neurological complications associated with the use of Efocaine recently have been reported to us.

REPORT OF CASES

CASE 1.—On March 29, 1953, a 65-year-old white man had ligation of a right popliteal aneurysm under spinal anesthesia. Following recovery from anesthesia, the patient noted severe pain in the lower leg and foot. Although he could move the foot, the skin was pale, cold, and obviously ischemic. On the first postoperative day, March 30, 1953, a right paravertebral lumbar sympathetic nerve block was done of the first, second, and third lumbar segments with 8 cc. of 1.5% piperocaine (Metycaine) hydrochloride followed by 2 cc. of Efocaine in the second and third lumbar areas. The patient noted immediate pain relief, but was unable to move either leg. Examination revealed skin anesthesia to the level of the 10th thoracic segment and complete motor anesthesia of both lower extremities. No noticeable recovery was noted over a four-month period. On April 4, 1953, the right leg was amputated for gangrene of the foot.

Comment.—It was the opinion of the neurosurgical consultant that a transverse myelitis at the level of the tenth lumbar segment had occurred secondary to the injection of Efocaine.

CASE 2.—H. G. C., a 22-year-old white man, was admitted to the hospital on June 11, 1952, with the chief complaint of cough and weakness. Three and six months before admission he experienced severe pulmonary hemorrhages. Bronchograms revealed bronchiectasis in the lower lobe and linguala of the left lung and a slight suggestion of bronchiectasis in the median basilar segment of the right lower lobe. On July 24, 1952, a left lower lobectomy with lingulectomy was carried out. At the completion of the operative procedure, prior to closure of the chest, an intercostal nerve block was done under direct vision, with use of Efocaine. One cubic centimeter of this mixture was injected at the inferior edge of each of five ribs—two ribs above and two ribs below the resected rib, at the angle of each rib approximately 3 to 5 cm. lateral to the head of each rib. A total of 5 cc. of Efocaine was injected.

The patient's immediate postoperative course, as regards the chest, was uneventful, but within 24 hours he complained of persistent numbness of the left leg. Urinary retention was noted on the third postoperative day, but subsided after catheter drainage. Because numbness of the left leg persisted, a complete neurological examination was carried out on July 30, 1952. At this time there was left thoracic analgesia. The left knee and ankle jerks were exaggerated, and there was decreased pressure sensation on the right. The clinical impression at this time was that there was a partial Brown Séquard syndrome at an indefinite level.

On Aug. 4, 1952, there was a definite left ataxia with a positive Babinski on the left. On Sept. 8, 1952, there were very active reflexes on the left. In the left leg the posterior column modalities were absent with marked impairment of touch, position, and vibratory sense. In the right leg spinal thalamic modalities were decreased below the knee (pain and temperature). There was still decreased pin prick sensation on the right below the knee. The strength of the left leg was now considered to be normal, but the patient walked with a slight limp. He was discharged on Nov. 14, 1952.

Comment.—The impression here was that partial and incomplete spinal cord involvement occurred secondary to the intercostal nerve injection with Efocaine.

CASE 3.—O. W. R., a 69-year-old white man, entered the hospital with the chief complaint of pain in the stomach dating back to the 30's. In 1947 this patient underwent a cholecystectomy, but continued to have pain after the procedure. In January, 1951, he became jaundiced and underwent surgery which "by-passed" his ulcer. Following this, his jaundice disappeared and he was asymptomatic for approximately one week, at the end of which time pain returned. This pain persisted and became excruciating. He entered the hospital on July 10, 1952, with a provisional diagnosis of carcinoma of the pancreas. On July 12, 1952, a right thoracic splanchnic nerve block was done with use of 10 cc. of 0.5% solution of lidocaine (Xylocaine) opposite

the 10th and 11th thoracic vertebrae for the preliminary injection, followed by 2 cc. of Efocaine in each space. The patient was in excellent spirits because of freedom from pain. That evening he ate his dinner, and it was noted that he could move his toes and feet and was able to turn himself. He was awakened from his sleep that night by severe pain in the lower part of the body and numbness of the legs. Because of his inability to void, on July 13, 1952, the patient was catheterized. On July 14, it was noted that he was paralyzed from the waist down and unable to raise himself or move his lower extremities. This condition persisted, and on July 18, 1952, an exploratory laparotomy was carried out under endotracheal pentothal-curare, nitrous oxide-oxygen anesthesia. The patient responded immediately after this anesthetic was administered. His postoperative course was good, except for a severe pain in the hip and lower extremities. On July 26 he was discharged and sent home by ambulance. From the time of his dismissal until his death on March 19, a marked weakness of the lower extremities persisted and he was unable to walk by himself.

Comment.—Spinal cord involvement here may have been due to a metastasis, but also may have been related to the injection of Efocaine.

GENERAL COMMENT

Since solutions injected into areolar tissue, fascial planes, or nerve trunks tend to spread into other areas, only solutions of known nontoxicity should be used. Procaine, while producing anesthesia of limited duration, has an extremely low neural toxicity. Since Efocaine has been shown to have a necrotizing effect on animal tissues, complications following its use in patients are to be expected.

SUMMARY AND CONCLUSIONS

Three cases have been presented in which spinal cord complications followed the use of Efocaine. These complications consisted of transverse myelitis in two cases, and Brown-Séquard syndrome, in one case, and followed intercostal nerve block in one, and sympathetic nerve block in two cases.

Since these complications are of such serious nature, the use of Efocaine should probably be limited to those areas where possible tissue damage is unimportant.

ADDENDUM

Since submission of this article for publication, five cases of spinal cord involvement associated with the use of Efocaine have been reported to us. Details of these cases and permission to publish them have been refused because of legal malpractice action. Also, a case report, "Death Following the Use of Efocaine," has been published by Angerer and associates (Angerer, A. L.; Su, H. H., and Head, J. R.: J. A. M. A. **153**:550 [Oct. 10] 1953).

CEREBRAL ARTERIOGRAPHY WITH SODIUM ACETRIZOATE (UROKON SODIUM) 30%

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AND
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THE FIRST use in this country of iodopyracet (Diodrast) for cerebral arteriography was reported by Gross [1] in 1940. The procedure has been used with increasing frequency to visualize cerebral circulation in many conditions, particularly in patients suspected of harboring intracranial aneurysms and tumors. Although this substance is relatively safe, the occasional occurrence of untoward reactions has been reported. Engeset [2] described two fatalities in a series of 100 patients but did not believe that death was primarily due to angiography. In 1949, Chusid, Robinson, and Margules-Lavergne,[3] in a report to the New York Society of Neurosurgery, noted two instances of transient hemiplegia following intracarotid injection of 35% iodopyracet, and 21 similar complications were mentioned in the discussion following this paper. Since then, other reports have been published.[4]

In searching for a substance of less toxicity, we thought the results of our preliminary clinical trials [5] with sodium acetrizoate (Urokon Sodium 30%) seemed promising enough to warrant further clinical investigation. The recent experience of Gass and Jacobson [6] also suggests that this is a fairly satisfactory contrast medium for cerebral arteriography. In their series of 62 arteriograms there was only 1 case of transient hemiplegia and aphasia.

From Washington University School of Medicine.

The Edward Mallinckrodt Institute of Radiology (Dr. Seaman); Department of Surgery, Division of Neurological Surgery (Dr. Schwartz).

1. Gross, S. W.: Cerebral Arteriography by Means of a Rapidly Excreted Organic Iodide, Arch. Neurol. & Psychiat. **44**:217, 1940.

2. Engeset A.: Angiography with Diodrast, Acta radiol. (Supp.) **56**:1, 1944.

3. Chusid, J.; Robinson, F., and Margules-Lavergne, M.: Transient Hemiplegia Associated with Cerebral Angiography (Diodrast), J. Neurosurg. **6**:466, 1949.

4. Olsson, O.: Cerebral Angiography: Tolerance for Contrast Media of Diodrast Type, J. Neurol., Neurosurg. & Psychiat. **12**:312, 1949. Culbreth, C. G.; Walker, A. E., and Curry, R. W.: Cerebral Angiography in "Brain Tumor Suspects," J. Neurosurg. **7**:127, 1950. Uhlein, A.: Cerebral Angiography, Proc. Staff Meet., Mayo Clin. **26**:133, 1951. Dunsmore, R.; Scoville, W. B., and Whitcomb, B. B.: Complications of Angiography, J. Neurosurg. **8**:110, 1951.

5. Seaman, W. B., and Schwartz, H. G.: Clinical Experience with Urokon Sodium 30 per cent (pH 7) for Cerebral Angiography, J. Missouri M. A. **49**:553, 1952.

6. Gass, H. H., and Jacobson, S. D.: The Use of Urokon in Cerebral Angiography: A Preliminary Report, Am. J. Roentgenol. **69**:428, 1953.

MATERIAL AND METHOD

During the past 18 months we have used sodium acetrizoate 30% in 297 intracarotid injections in 125 patients. Most of the injections were done by the percutaneous method, using local procaine or lidocaine (Xylocaine) anesthesia. The amount of acetrizoate used per injection ranged from 6 to 20 cc., with an average of 9 cc. Since the recent development of satisfactory equipment for simultaneous biplane serial roentgenography, only one injection is necessary to obtain lateral and frontal roentgenograms.[7] Because of the importance of visualizing the arteries of both cerebral hemispheres, two or more injections were done in 71 patients. The ages of the patients ranged from 4½ to 74 years, with 36 patients over 50 years old.

OBSERVATIONS

Immediate reactions to the injection were less than those usually observed with other contrast media. The visible flush of the skin, momentary muscular rigidity, and transient pupillary dilatation that invariably accompanied intra-arterial injection of other contrast media were absent when sodium acetrizoate 30% was used. Subjectively the patients still experienced a hot flash during the injection, occasionally most marked in the retro-orbital region.

Patients, no.	125
Injections, no.	297
Average number of injections per patient	2.37
Average amount of sodium acetrizoate per injection	9 cc.
Major reactions, no.	7
Major reactions, %	5.6
Minor reactions, no.	20
Minor reactions, %	16

Reactions following injection were divided into two categories, major and minor. The minor reactions were clinically insignificant and consisted of a brief period of confusion in 2 patients, a momentary hemiparesis in 1 patient, and transitory burning sensation in the face and retro-orbital area in 17 patients. Clinically significant reactions occurred in seven patients, a case incidence of 5.6%, and carotid injection incidence of 2.3%. In one patient who died within 24 hours after angiography, autopsy disclosed a brain-stem glioma in which hemorrhage had occurred. During angiography this patient was maintained in a position of extreme hyperextension, and it is conceivable that bleeding into the tumor might have been related to traumatic factors or to interference with venous return.

CLINICAL ABSTRACTS OF PATIENTS IN WHOM MAJOR REACTIONS OCCURRED

CASE 1.—G. L., a 55-year-old man, entered Barnes Hospital with a history of tinnitus of five months' duration. One month after onset of the tinnitus, diplopia, right-sided numbness, right hemiparesis, and a left facial weakness developed. A few days prior to hospital entry he had noted mild dysphagia and dysarthria.

Examination revealed right hemiparesis, right hemihypesthesia, left abducens paralysis, and a moderate left facial weakness. There was no definite involvement of the 9th, 10th or 11th cranial nerves. Angiography of the right vertebral artery, using both iodopyracet (10 cc.) and 30% sodium acetrizoate (20 cc.), was attempted without success. Four days later vertebral arteriography was again attempted by the retrograde carotid injection of 20 cc. of 30% sodium

7. Seaman, W. B.; Scott, W. G., and Henry, W. D.: Simultaneous Biplane Cerebral Roentgenography, Am. J. Roentgenol, **70**:445, 1953.

acetrizoate, with the patient in a position of extreme hyperextension. Several minutes after the injection the patient vomited and became unresponsive; decerebrate rigidity developed. Ventricular drainage disclosed bloody fluid under increased pressure. The patient died 24 hours after angiography. At autopsy a glioma of the pons was found, with hemorrhage into the substance of the tumor.

CASE 2.—J. P., a 55-year-old woman, entered the hospital because of increasing left-sided weakness of two months' duration. Examination disclosed a moderate left hemiparesis and a blood pressure of 168/88. Three days later percutaneous arteriography was done with use of local procaine anesthesia. Seven minutes following the injection a complete left hemiplegia developed, with conjugate deviation of the eyes and loss of consciousness. Twenty-four hours later the patient was comatose and in a decerebrate condition, with a fixed dilated right pupil and the eyes in extreme lateral deviation. Craniotomy disclosed a 2 cm. metastatic tumor high in the right parietal region. The patient died the day following craniotomy.

CASE 3.—G. L. K., a 57-year-old woman, first entered the hospital because of blurred vision of three weeks' duration. Examination disclosed right medial rectus weakness, hypertension (160/90), and evidence of arteriosclerosis of the retinal vessels.

Six months later she had several generalized convulsions followed by right hemiplegia and aphasia. This condition slowly subsided, and at hospital entry one week later the aphasia had cleared, although there was still moderate right-sided weakness with a central type of right facial paresis, right hemihypalgesia, and hypesthesia. The spinal fluid was normal. Percutaneous arteriography of the left carotid artery was carried out with the use of local procaine anesthesia. One injection of 10 cc. of 30% sodium acetrizoate was given without untoward reactions. After prolonged manipulation of the needle for a second injection the patient experienced stertorous respirations, aphasia, and a complete paralysis of the right upper extremity. No loss of consciousness occurred. Two days later she was able to speak but there was only minimal improvement in her paralysis.

CASE 4.—G. J., a 53-year-old white man, entered the hospital because of suboccipital headaches and stiff neck of five days' duration. Examination revealed a lethargic man with a stiff neck. Lumbar puncture revealed an initial pressure of 450, with xanthochromic spinal fluid containing many red blood cells. The patient's hospital course was characterized by shifting neurological findings. A few hours after entry he experienced a left facial weakness, with weakness of the left arm and leg and a left Babinski reflex. These findings disappeared the next day except for the Babinski reflex, which persisted. On the third hospital day a percutaneous arteriogram was done, with the use of local anesthesia, with two injections of 12 cc. of 30% sodium acetrizoate into the right carotid artery. The patient tolerated the procedure well. Two days later a left carotid arteriogram was done, using 15 cc. of 30% sodium acetrizoate, which demonstrated an aneurysm of the left internal carotid artery. About an hour following this second arteriogram a mild right hemiparesis with motor aphasia developed, which persisted until the time of surgery, six days later. The patient died three days after intracranial ligation of the neck of the aneurysm.

CASE 5.—D. M., a 29-year-old pregnant Negro woman, had a four week history of left-sided headache. Examination revealed a left ophthalmoplegia. The spinal fluid was not bloody. Left percutaneous carotid arteriography was performed, with the use of local procaine anesthesia, using 12 cc. of 30% acetrizoate. An aneurysm measuring 5 by 5 by 9 mm. arising from the distal left internal carotid artery at the site of the origin of the posterior communicating artery was demonstrated. At the conclusion of the procedure, right hemiparesis and marked aphasia were noted. During the following six hours two generalized convulsions lasting 20 to 30 seconds each occurred. Over the next six days the hemiparesis and aphasia slowly cleared. Two weeks after the first arteriogram a percutaneous injection of the right carotid artery was done, using 10 cc. of 30% sodium acetrizoate. The arteriogram showed nothing abnormal, and the patient had no reaction. She refused surgery and was discharged with no residual hemiparesis or aphasia.

CASE 6.—J. McD., a 22-year-old white man, had a condition diagnosed as acromegaly. For six months he had complained of blurred vision, bitemporal headaches, and progressive drowsiness. Examination at the time of hospital entry revealed no abnormalities except for ptosis of the right eyelid and diminished visual acuity bilaterally without papilledema or optic atrophy.

Examination of the visual fields was not satisfactory but was thought to indicate a generalized field constriction. Roentgen examination of the skull revealed the typical manifestations of acromegaly, with large frontal sinuses, elongated mandible, and ballooning of the sella turcica. On the third hospital day he became lethargic and nauseated and complained of a severe pain in the right eye and exacerbation of his headaches. Examination revealed a dilated right pupil, slight blurring of the right optic nerve, and paresis of the right third nerve. The clinical impression was hemorrhage into the pituitary tumor with consequent rapid enlargement. Spinal paracentesis disclosed an initial pressure of 200 mm. and spinal fluid containing 89 mg. of protein per 100 cc. and 1,700 red blood cells. The following day paresis of the right third, fourth, and sixth, and first division of the fifth cranial nerves developed, accompanied by stiffness of the neck. On the fifth hospital day percutaneous cerebral arteriography was performed, with the area under local lidocaine anesthesia, with the injection of 11 cc. of 30% sodium acetrizoate into the right cartoid artery. The roentgenograms showed lateral displacement of the distal portion of the right internal carotid artery in the frontal projection, while in the lateral views the distal internal carotid was displaced anteriorly and superiorly. Immediately after the injection a left hemiparesis was observed, which completely disappeared after an interval of 30 minutes. Craniotomy disclosed a large pituitary tumor with evidence of recent hemorrhage.

CASE 7.—C. B., a 64-year-old white man, entered the hospital on Dec. 31, 1952, because of the sudden onset of severe bifrontal and retro-orbital headaches three days before. Neurologic examination revealed nothing abnormal except for moderate lethargy and stiff neck. The spinal fluid was xanthochromic and contained 1,060 red blood cells and 71 mg. of protein per 100 cc. On Jan. 3, 1953, a right percutaneous carotid arteriography was done, with the area under local lidocaine anesthesia, using 11 cc. of 30% sodium acetrizoate. No untoward reactions were noted. Initial films were not diagnostic, and a second injection of 11 cc. of 30% sodium acetrizoate was done 30 minutes later. This revealed no abnormalities, but a left hemiparesis, which was most marked in the left upper extremity, and a left Babinski reaction developed. The hemiparesis disappeared completely in 12 hours, and the patient was well except for a mild right-sided headache. A chest roentgenogram showed destructive lesions in the left seventh rib and in the third thoracic vertebra. Biopsy of the rib lesion disclosed anaplastic carcinoma that was thought to be of prostatic or renal origin. On Jan. 13, a flaccid left hemiparesis developed, with weakness of the left seventh cranial nerve, right-sided headache, and stiff neck that was still present at the time of the patient's discharge on Feb. 6, 1953. It was assumed that he had a cerebral metastasis.

COMMENT

Although one patient (Case 1) in our series died shortly after angiography, it is felt that the autopsy findings constituted an adequate explanation of his death and that it was unrelated to the use of a contrast medium. The causal relationship of the development of hemiplegia to the administration of sodium acetrizoate is not clear, but among the possible mechanisms are (1) alteration of cerebral vascular permeability, (2) direct cytotoxic effect on the central nervous system, (3) direct irritative effect of contrast material and/or arterial puncture. Experimental data suggest that alteration of the endothelial capillary membrane is probably the most important of these factors.[8] Bassett and his associates [8a] have shown that the degree

8. (*a*) Bassett, R. C.; Rogers, J. S.; Cherry, G. R., and Gruzhit, C.: The Effect of Contrast Media on The Blood-Brain-Barrier, J. Neurosurg. **10**:38, 1953. (*b*) Bloor, B. M.; Wrenn, F. R., and Margolis, G.: An Experimental Evaluation of Certain Contrast Media Used for Cerebral Angiography, J. Neurosurg. **8**:585, 1951. (*c*) Broman, T., and Olsson, O.: Experimental Study of Contrast Media for Cerebral Angiography with Reference to Possible Injurious Effects on the Cerebral Blood Vessels, Acta radiol. **31**:321, 1949. (*d*) Smith, G. A.; Caudill, C. M.; Moore, G. E.; Peyton, W. T., and French, L. A.: Experimental Evaluation of Cerebral Angiography, J. Neurosurg. **8**:556, 1951. (*e*) Tarlov, I. M., and Rosenberg, M.: Cerebral Angiography with Iodopyracet Injection U.S.P. (Diodrast), A.M.A. Arch Neurol. & Psychiat. **67**:496, 1952.

of vascular damage is directly proportional to the concentration and quantity of contrast material which is in contact with the endothelium and that repeated fractional doses have a cumulative effect. This has also been our experience and emphasizes the importance of keeping the number of injections per patient to a minimum, and not using contrast material of high concentrations. Sodium acetrizoate 70% should not be used for cerebral angiography.

In two patients the reactions consisted of accentuation of a hemiparesis that had previously been present. In another patient with metastatic carcinoma the hemiplegia recurred 10 days after the postangiographic hemiplegia had disappeared. Five of the seven patients with complications were in the sixth and seventh decades; three were hypertensive, which probably increased the hazards of arteriography.

SUMMARY

Intracarotid injection of sodium acetrizoate (Urokon Sodium) 30% has been used in obtaining 297 cerebral angiograms in 125 patients. Subjective discomfort following the injection was less than usually observed with other contrast media. In this series there were seven major neurological complications. Although not ideal, it is concluded that sodium acetrizoate 30% is a satisfactory contrast medium for cerebral arteriography.

QUALITATIVE DIFFERENCE BETWEEN LEVOEPINEPHRINE AND LEVOARTERENOL

Experimental Demonstration

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WHEN TAINTER, Tullar, and Luduena [1] reported, in 1948, the successful synthesis of levoarterenol, a smouldering controversy flared anew. Since Oliver and Shaefer,[2] in 1895, observed that extracts of the adrenal medulla gave a vasopressor effect when administered intravenously to animals, a host of investigators have interested themselves in the apparent paradox of the inhibitory action of epinephrine in minimal amounts as compared with an excitatory action in larger amounts. Barger and Dale,[3] in 1910, speculated that the sympathetic effector substance might not be epinephrine but, rather, a closely related catechol with a primary amine side-chain. Cannon [4] proposed the concept of two forms of sympathetic effector substances, an inhibitor and an excitor form, which he called sympathin I and sympathin E, respectively. Bacq [5] suggested the possibility that arterenol might be sympathin E, and Blaschko [6] postulated that arterenol might be the precursor of epinephrine. In recent years numerous reports have appeared supporting or denying the contention that arterenol is a vasopressor substance, while epinephrine is a vasodepressor substance. Cannon and Lyman,[7] Dale and Richards,[8] Clark,[9] and Allen [10]

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1. Tainter, M. L.; Tullar, B. F., and Luduena, F. P.: Levo-Arterenol, Science **107**:39-40 (Jan. 9) 1948.

2. Fulton, W. H.: A Textbook of Physiology, Ed. 16, Philadelphia, W. B. Saunders Company, 1949, p. 1135.

3. Barger, G., and Dale, H. H.: Chemical Structure and Sympathomimetic Action of Amines, J. Physiol. **41**:19-59 (Oct. 11) 1910.

4. Cannon, W. B., and Rosenblueth, A.: Autonomic Neuro-Effector Systems, New York, The Macmillan Company, 1937, Chap. 14, Sensitization of Autonomic Effectors to Chemical Mediator, pp. 187-199.

5. Bacq, Z. M.: La pharmacologie du système nerveaux autonome, et particulièrement du sympathique, d'après la theorie neurohumorale, Ann. physiol. **10**:467-553, 1934.

6. Blaschko, H.: Activity of l(—)-Dopa Decarboxylase, J. Physiol. **101**:337-349 (Nov. 30) 1942.

7. Cannon, W. B., and Lyman, H.: The Depressor Effect of Adrenalin on Arterial Pressure, Am. J. Physiol. **31**:376-398 (March 1) 1913.

8. Dale, H. H., and Richards, N.: Depressor (Vasodilator) Action of Adrenaline, J. Physiol. **63**:201-210 (Aug.) 1927.

9. Clark, G. A.: Vaso-Dilator Action of Adrenaline, J. Physiol. **80**:429-440 (Feb. 28) 1934.

10. Allen, W. J.: Action of Adrenaline, Ephedrine, and Methedrine on Circulation in Man, Clin. Sci. **6**:269-279 (Feb.) 1948.

are among those who have reported a distinct vasodilator action of epinephrine, while a multitude of others has been quick to refute these claims. Most recently, Goldenberg and his associates [11] reported that epinephrine, in doses sufficient to cause significant hypertension, was found to act as an over-all vasodilator, as well as a powerful cardiac stimulant. Arterenol, on the other hand, was found to act primarily as a vasoconstrictor. Wakim and Essex,[12] however, reported that the two agents produced immediate increases in blood pressure and blood flow at about the same rate for equivalent doses of the drugs. The question "Is there a qualitative difference between epinephrine and arterenol?" remains to be answered.

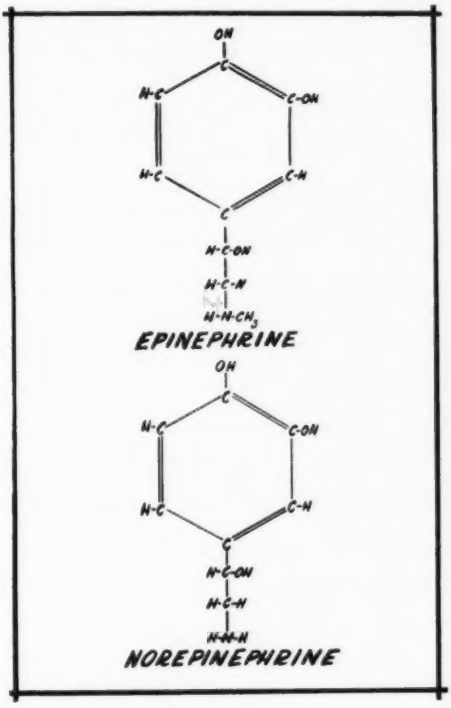

Chart 1.

In a philosophical sense the proposal that a biologically active substance acts in one manner in a low concentration and in a directly opposite manner in a high concentration does not seem orderly. Yet, some evidence seems to indicate that such is the case with epinephrine. If, however, the evidence can be interpreted somewhat differently, one can perhaps still satisfy the desire to believe that nature is orderly in all things. With the evidence which we have gathered, we hope to stimulate others to entertain such an interpretation.

11. Goldenberg, M., and others: Hemodynamic Response of Man to Nor-Epinephrine and Epinephrine, and Its Relation to Problem of Hypertension, Am. J. Med. **5**:792-806 (Dec.) 1948.

12. Wakim, K. G., and Essex, H. E.: Comparison of the Circulatory Effects of Epinephrine and Norepinephrine, Circulation **5**:370-379 (March) 1952.

Certain generally accepted concepts seem not to enter into the controversy, and for the moment we shall concern ourselves with these.

1. In 1904 Stolz [13] synthesized epinephrine, and the basic structure of the substance has been established, as indicated in Chart 1.

2. Arterenol, as synthesized by Tainter, Tullar, and Luduena,[1] differs from epinephrine in that it lacks the methyl group on the amine side-chain (Chart 1).

3. Transmethylation occurs freely in the body.[14]

4. Levoisomers are generally more active than dextroisomers or racemic mixtures.

With these concepts in mind we began a study comparing the effects of levoarterenol and levoepinephrine on arterial, portal venous, and right auricular pressures and on cardiac rate. The agents were administered by way of the portal vein or the jugular vein, and, because the levoisomers of the agents are the most active, the study was confined exclusively to them.

TECHNIQUES

Twenty-four healthy mongrel dogs weighing from 15 to 22 kg. were used; they were anesthetized with 5 mg. per kilogram of veterinary pentobarbital (Nembutal).

Splenectomies were performed to obviate the possible complicating factor of action of the agents on the spleen.

Arterial pressure was obtained by use of a mercury U-tube manometer connected by a closed system to a cannula in the carotid artery.

Portal pressure was obtained by use of a spinal manometer filled with saline and connected to an indwelling polyethylene catheter in the portal vein by way of the splenic vein stump.

Right auricular pressure was obtained by use of a similar manometer connected to a catheter in the right auricle by way of the jugular vein.

Cardiac rate was obtained electrocardiographically.

Synthetic levoarterenol bitartrate and levoepinephrine bilartrate [15] were administered by way of polyethylene catheters separately placed in the portal and jugular veins.

A preliminary autopsy study on dogs killed in other studies was carried out to determine placement of the right auricular catheter and the topographical "zero" point of venous pressure taken as the most dependent portion of the blood column in the right auricle.

The study was divided into two groups. Thirteen dogs were first studied with single injections into the respective veins, then 11 dogs were studied with continuous infusions into each system.

FINDINGS

The pertinent results in Group 1 are illustrated in Chart 2 and in Table 1. Arterenol regularly caused an elevation in both portal and arterial pressure in the dose range used (10 to 12 γ per kilogram). As might be anticipated, there was a greater response in arterial pressure when the agent was administered systemically, while portal pressure showed a correspondingly lesser response. As the effect of the agent was dissipated, the pressures gradually returned to the original base line. Epinephrine, in the same dose range, however, acted very differently. When it was administered by way of the portal vein, an immediate rise in portal pressure was noted, but arterial pressure either showed no change or fluctuated erratically. When

13. Stolz, R.: Über Adrenalin und Alkylaminoacetobrenzcatechie, Ber. deutscher chem. Gesellsch. **37**:4149-4155, 1904.

14. du Vigneuad, V.: Significance of Labile Methyl Groups in Diet, and their Relation to Transmethylation, Harvey Lect. **38**:39-42, 1942-1943.

15. Arterenol (Levophed) and epinephrine (Suprarenin) were supplied by the Department of Medical Research, Winthrop-Stearns, Inc., New York.

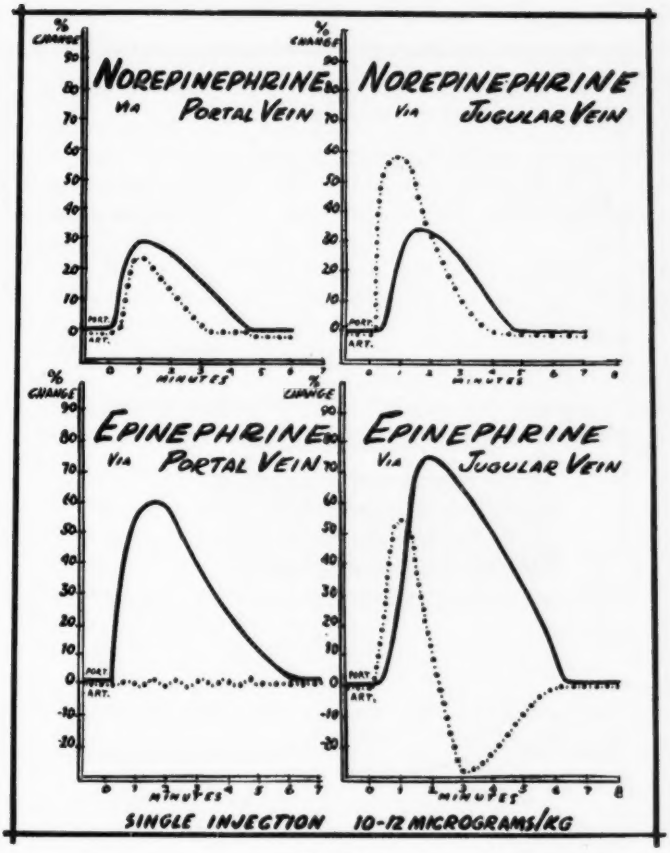

Chart 2.

TABLE 1.—*Single Injection**

Group	Agent	Route	Portal	Systemic
1	Lag in action after administration			
	Arterenol	Portal	0	17
	Arterenol	Jugular	21	0
	Epinephrine	Portal	0	15
	Epinephrine	Jugular	19	0
2	Summit of rise in pressure			
	Arterenol	Portal	56	47
	Arterenol	Jugular	96	55
	Epinephrine	Portal	83	0
	Epinephrine	Jugular	104	56
3	Secondary fall in pressure			
	Arterenol	Both	0	0
	Epinephrine	Portal	0	0
	Epinephrine	Jugular	0	179
4	Return of pressures to base line			
	Arterenol	Portal	264	185
	Arterenol	Jugular	290	223
	Epinephrine	Portal	370	300
	Epinephrine	Jugular	375	367

* Time relationships are given in seconds in terms of averages for each group.

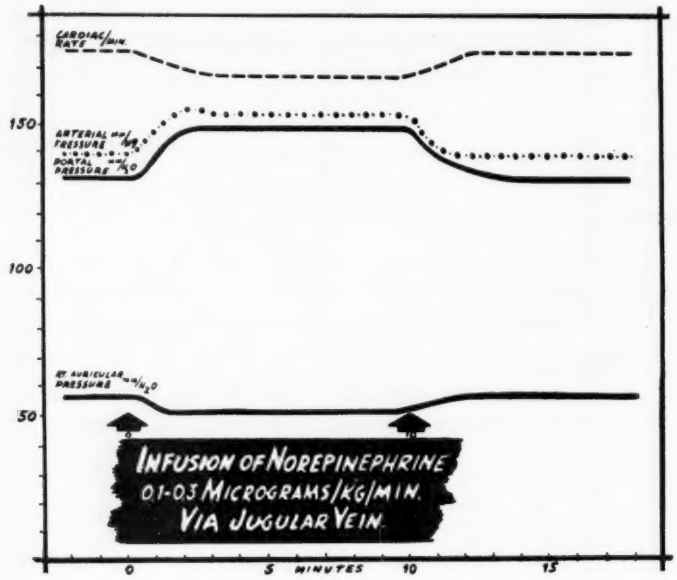

Chart 3.

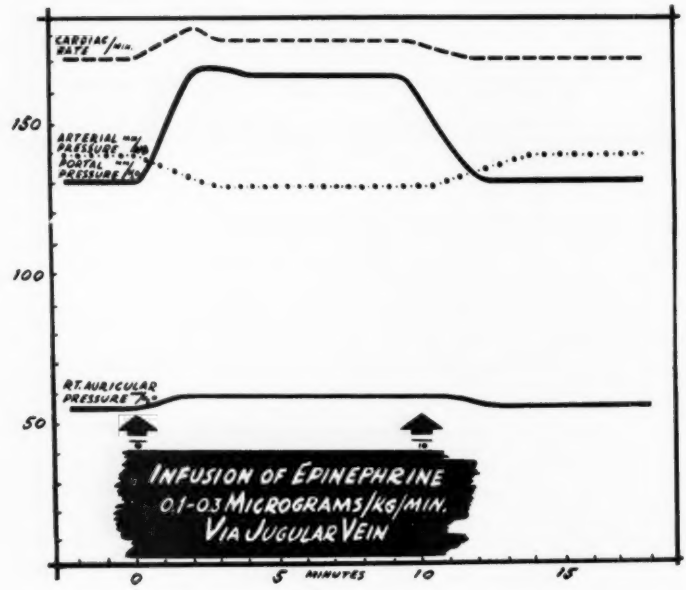

Chart 4.

administered systemically, epinephrine caused significant elevations in both portal and arterial pressure. Then, while portal pressure slowly returned to base line, arterial pressure dropped precipitously below base line before gradually returning to the original normal pressure. Graduated doses of each agent were then tried, as high as 65 γ per kilogram; the patterns were noted to be accentuated but essentially unchanged, except for the fact that three animals went into shock with massive doses of epinephrine. In these instances the arterial pressure continued to zero on the secondary fall.

Cardiac rate, studied on two occasions in this group, revealed a tachycardia when epinephrine was administered by either route and a bradycardia when arterenol was administered in the same manner. The effect was greater in each instance when the agent was administered systemically.

In Group 2 the pertinent findings are illustrated in Charts 3 and 4 and in Table 2. The dose ranged from 0.16 to 0.34 γ per kilogram per minute. When doses as high as 3.0 γ per kilogram per minute were tested, the basic patterns were accen-

TABLE 2—*Continuous Infusion*

Agent	Route	Percentage Changes* Arterial Pressure	Portal Pressure	Cardiac Rate	Rt. Auricular Pressure
Arterenol	PV	5	9	—2	3
Arterenol	JV	9	11	—10	—4
Epinephrine	PV	—2	32	2	4
Epinephrine	JV	—7	15	4	—1

Time Relationships, in Minutes*

		Arterial Pressure		Portal Pressure		Cardiac Rate		Rt. Auricular Pressure	
Agent	Route	Max. Change	Return Base	Max. Change	Return Base	Max. Change	Return Base	Max. Change	Return Base
Arterenol	PV	3.6	3.6	3.7	3.4	3.0	3.0	1.7	1.8
Arterenol	JV	3.6	3.5	3.9	3.7	2.7	3.0	1.6	1.8
Epinephrine	PV	4.4	5.0	3.1	3.9	1.5	1.5	3.8	3.9
Epinephrine	JV	4.9	7.3	4.4	3.9	2.2	3.0	3.9	3.9

* Given in terms of averages for each group.

tuated but otherwise not essentially altered. Portal pressure was elevated by each agent irrespective of the route of administration. Arterial pressure was consistently elevated by arterenol but depressed by epinephrine. Cardiac rate was slowed by arterenol, while epinephrine caused a transient tachycardia. Right auricular pressure showed a slight variable response, which was not deemed significant. The time interval until a maximum response of arterial pressure was attained was significantly greater with epinephrine than with arterenol, and the interval from the time the infusion was discontinued until the arterial pressure returned to base line was significantly greater with epinephrine. No significant differences in time relationships were noted in the other factors recorded.

COMMENT

The findings indicate that the two substances produce different effects; the mode of action then becomes the prime question. Is it reasonable to suppose that one substance is destroyed more rapidly than the other, or that one is partially oxidized to a relaxing form, or that transmethylation occurs, changing one form into the other?

For the sake of discussion, let us say that arterenol is a pure vasoexcitor substance and that epinephrine is a pure vasoinhibitor substance. One may then speculate that transmethylation occurs, possibly in the liver, and transforms epinephrine into arterenol as the body requires a vasoexcitor substance to maintain normal vascular tone. A normal relationship of approximately 4 parts of epinephrine to 1 part of arterenol has been demonstrated to exist in natural extracts of the adrenal medulla.[16] If extracorporeal quantities of either component are introduced to disturb this ratio, it might be of interest to observe what happens to vascular tone as reflected in pressure relationships; this we have attempted to do. In order to appreciate the possible mechanisms which operate to effect pressure changes, let us consider the vascular dynamics involved. In a given area the blood pressure depends primarily upon the volume inflow and the resistance to outflow of that area. In the closed portal bed the volume inflow is governed mainly by the state of vascular tone of the splanchnic arteriolar bed, while the resistance to outflow depends upon the state of vascular tone of the portal venules, the hepatic venules, the vena-caval back-pressure, and, possibly, the resistance afforded by the hepatic arteriolar bed.[17] The systemic volume inflow depends upon the cardiac output, and the resistance to outflow depends upon the state of vascular tone of the systemic arteriolar bed.

When arterenol is introduced into either the portal or the systemic circulation, a rise in portal and arterial pressure is effected which corresponds roughly to the magnitude of the dose given and can be explained on the basis of a pure vasoconstrictor action. If epinephrine acts upon the peripheral systemic arteriolar bed as a dilating agent, the fall in pressure which has been noted can be explained in a reduction in the resistance to outflow. Then, if upon reaching the liver, epinephrine is demethylated and thus transformed into arterenol, a vasoconstriction of the hepatic venules causes an increased resistance to portal outflow as the newly manufactured arterenol acts upon the first area it reaches. Therefore the elevation in portal pressure can be explained. In no event can the changes in right auricular pressure, which represents systemic venous return and also vena-caval back-pressure, or the changes in cardiac rate be construed to account for the changes in portal and arterial pressure which were recorded.

SUMMARY

A qualitative difference has been demonstrated between levoarterenol and levoepinephrine.

A thesis has been suggested to account for this difference, that is, that arterenol is a vasoexcitor substance while epinephrine is a vasoinhibitor substance and that demethylation at some site in the body, possibly the liver, effects a transformation of epinephrine into arterenol as the vascular system demands to maintain normal tone.

Dr. H. L. Graff, Mary McPherson, and Ruth Hanavan gave technical assistance.

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STUDIES OF COMBINED VASCULAR AND NEUROLOGIC INJURIES

III. The Effect of Arterial Ligation and Sympathetic Denervation upon Return of Function after Crushing of Sciatic Nerve of the Cat

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PREVIOUS studies with domestic albino rats have shed some light upon the interrelationship of somatic and sympathetic activity and paralysis, upon the circulatory and nutritional status of the extremities, and upon the effect of adequacy of blood supply on somatic neural repair. It was found that interruption of the common iliac and common femoral arteries resulted in a high incidence of ischemic paralysis and a low incidence of tissue necrosis.[1] Recovery of function from this ischemic paralysis was hastened by homolateral sympathetic ganglionectomy. Section of the sciatic nerve in combination with such arterial interruption was followed by a marked delay in return of neurologic function and a striking increase in the occurrence of tissue necrosis. Sympathectomy greatly reduced the frequency of necrosis of tissue. Division of the common femoral and iliac arteries prolonged significantly the interval before return of neurologic function after crushing of the sciatic nerve, while sympathetic denervation shortened appreciably the period before return of function both in animals with crushed sciatic nerve and arterial interruption and in animals with crushed sciatic nerve and intact main arterial pathways.[2]

The present study is concerned with similar problems in the cat.

MATERIALS AND METHODS

Mongrel cats of varying sizes and ages were used. With the animals under intraperitoneally administered pentobarbital anesthesia and with the use of aseptic technique the distal portion of the sciatic nerve immediately proximal to its bifurcation was exposed in the upper portion of the popliteal space and was crushed for 15 seconds with a modified Kelly clamp, the jaws of which were polished and cut to a width of 4 mm. The nerve was crushed at the same level in all animals and the distance between the site of crushing and the distal end of the os calcis was measured in each case. In some animals the homolateral common iliac and common femoral arteries were divided between fine silk ligatures. In others a homolateral lumbar sympathetic

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This study was aided by a grant from the National Institute of Neurological Diseases and Blindness of the National Institute of Health, United States Public Health Service.

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ganglionectomy was carried out extraperitoneally. In still others both arterial division and sympathectomy were performed. The adequacy of sympathectomy was checked by postmortem examination in each animal. The animals did not gnaw at or otherwise injure their denervated extremity. They were kept in cages in a room maintained at 72 F. and were fed a standard laboratory diet. Each was observed daily until return of full neurologic function was judged to be complete by normal fanning of toes.

OBSERVATIONS

Sciatic Crush.—This control group consisted of 20 animals which ranged in weight from 4 to 9 lb. (1.8 to 4.1 kg.) and averaged 5¾ lb. (2.7 kg.). The distance from the site of crushing to ankle varied from 9 to 13 cm. and averaged 10.75 cm. Recovery of full neurologic function took place in from 72 to 125 days; the mean period was 93.6 and the median, 90.5 days. The days required for recovery per centimeter of nerve between the site of crushing and ankle averaged 8.74.

Sciatic Crush and Arterial Ligation.—There were 18 animals in this group. They varied in weight from 3 to 8½ lb. (1.4 to 3.9 kg.) and averaged 6.65 lb. (3 kg.). The distance from site of crush to ankle ranged from 7.16 to 14.6 cm. and

Comparison of Rate of Return of Nerve Function After Crushing the Sciatic Nerve and with Concomitant Arterial Injury, Sympathectomy, or Both

Operative Procedure	No. of Animals	Average Weight, Lb.	Days Between Nerve Injury and Return of Function		Cm. Between Site of Crush and Ankle	Period of Recovery in Days per Cm. of Nerve Between Site of Crush and Ankle
			Mean	Median		
Sciatic crush	20	5.75	93.6	90.5	10.75	8.74
Sciatic crush and arterial ligation	18	6.65	97.8	97	10.97	8.91
Sciatic crush, arterial ligation and sympathectomy	20	6.7	89.4	91.5	11.37	7.83
Sciatic crush and sympathectomy	20	6.8	90.5	87.5	11.52	7.86

averaged 10.97 cm. Recovery of function was noted in from 72 to 146 days; the mean was 97.8 and the median 97 days. The days elapsing between nerve injury and recovery of function per centimeter of nerve from site of injury to ankle averaged 8.91.

Sciatic Crush, Arterial Ligation, and Sympathectomy.—Twenty animals composed this group. They ranged in weight between 5 and 12 lb. (2.3 and 5.4 kg.) and averaged 6.7 lb. (3.1 kg.). The distance between site of crushing and ankle varied from 9 to 14.5 cm. and averaged 11.37 cm. Neurologic recovery took place in from 66 to 105 days, the mean being 89.4 and the median 91.5. The number of days required for recovery per centimeter of nerve between site of injury and ankle averaged 7.83.

Sciatic Crush and Sympathectomy.—There were 20 animals in this group. Their weights ranged from 4 to 9.5 lb. (1.8 to 4.4 kg.) and averaged 6.8 lb. (3.1 kg.). The distance between level of neural injury and ankle varied from 9.5 to 13 cm. and averaged 11.52 cm. Return of full neurologic function was noted in from 72 to 127 days, the mean being 90.5, the median 87.5. The number of days required for recovery per centimeter of nerve from site of crush to ankle averaged 7.86.

RESULTS

These results are tabulated in the Table. The mean and median periods between sciatic injury and return of function were somewhat longer in the group in which arterial ligation was performed and somewhat shorter in those treated by sympathectomy, regardless of whether the main arterial blood supply was interrupted or left intact. The same trend was noted when the results were studied with reference to the period of recovery in days per centimeter of nerve between site of crushing and ankle. These trends were not, however, found to be of statistical significance when analyzed by determination of the *t* ratio.

SUMMARY AND CONCLUSIONS

The remarkable influence of the circulatory status of the limb and the presence or absence of sympathetic activity upon the rapidity of return of neural function after crushing the sciatic nerve of the rat prompted us to make a similar study in another species. The cat was selected because of the lability of vascular tonus in this species as evidenced by the responsiveness of the temperature of the foot pad to exposure of the animal in a mildly cool atmosphere and the comparative stability of the skin temperature of the sympathetically denervated limb under such conditions.[3] The cat, however, proved an unsuitable animal from several other standpoints. In contrast to the situation with rats, where a single breed of relatively constant size and age was obtainable, the cats available for study varied widely in breed, size, and age. Furthermore, though return of nerve function was easily established in the rat by determination of the presence of normal fanning of the toes, this end-point was found to be less precise in the cat. In addition, the circulation of the cat's hindlimb is apparently less markedly affected by division of the common femoral and iliac arteries than is that of the rat. Twenty-three of 26 rats subjected to interruption of these arteries manifested at least transient ischemic paralysis,[1] while this proved to be the case in only 3 of 10 cats.

Under the circumstances, with animals of varying breed, weight, and age and with difficulty in establishing precisely the time of full return of neural function, it is perhaps more surprising that the same trends were noted in the cat as had been previously established in the rat than that these trends did not prove significant according to statistical analysis. This trend was observed in comparing the mean period between nerve injury and recovery, the median period, and the mean period divided by the length of nerve between site of crushing and ankle.

In final analysis the clinical validity of the conclusions drawn from the earlier studies in rats must be established or refuted, as must those from all animal experiments, by carefully controlled observations in man.

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MANAGEMENT OF AIRWAY IN ACUTE HEAD INJURY

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IN SPITE of the remarkable advances made in the emergency management and definitive treatment of the injured, critical analysis of reported series still reveals a high mortality rate among those patients who are seriously hurt. We could correctly assume that there are morphologic and physiologic limits to the extent of injury which are compatible with recovery; generally and specifically, these would be difficult to delineate. However, it would seem that with a large mortality, there could be some room for improvement. In particular, the past decade has witnessed an increased emphasis on the maintenance of a patent airway in the treatment of all types of trauma. With respect to cases of head injury, this is certainly one aspect which deserves further consideration.

Respiratory obstruction with resultant asphyxia has two components[1]: first, a reduced pulmonary ventilation capacity evidenced clinically as dyspnea; and second, hypoventilation. The latter produces hypercapnia (increased circulating CO_2 levels) and anoxemia (decreased O_2 levels), which result in acidemia and severe acidosis, both respiratory and metabolic. Early, this serves as a stimulus to increase respiratory effort until a critical point is reached. Subsequently this stimulus changes to inhibition, with eventual respiratory collapse. Anatomically, this results in permanent changes in the central nervous system, even after short periods of time.[2] There may be local respiratory tract complications of congestion, atelectasis, and the sequelae, pneumonitis, "drowned lung" and lung abscess.[3] Thus there is created a vicious cycle[4]: respiratory obstruction; dyspnea producing increased intrathoracic pressure, which contributes to the increased intracranial pressure; hypercapnia and anoxemia, producing further cerebral edema and eventual permanent cerebral damage. This cycle must be interrupted by prompt and direct action to relieve the respiratory obstruction.

The most effective way to achieve this is by endotracheal intubation.[5] Four forms are generally available: (1) the single catheter method employing a no. 16

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French catheter; (2) the "tracheobronchial toilet," using a small catheter through a wide bore tube; (3) bronchoscopy; (4) tracheostomy. Our initial experiences with the first three forms were not consistently successful (Table 1). All 10 patients succumbed to the combined effects of their head and concomitant injuries and complications thereof. Each, additionally, had evidences of respiratory tract obstruction. We, therefore, turned to tracheostomy with better results, albeit the percentage of mortality was still great (Tables 2 and 3). However, it was our observation that there was a definite improvement in all patients on whom this type of therapy was instituted. We succeeded in salvaging six patients whom we felt would have certainly died if tracheostomy with relief of respiratory obstruction had not been accomplished.

TABLE 1.—*Ten Patients with Endotracheal Suction Who Died*

Patient	Age	Sex	Head Injury	Complications	Coma Hr.	Survival Hr.
J. D.	60	M	Cerebral contusion	.....	66	66
R. S.	21	M	Compound fracture of skull; cerebral contusion	Multiple fractures of femur	23	23
J. M.	32	F	Compound comminuted fracture of skull; epidural hematoma	Illuminating gas intoxication	12	12
P. B.	60	M	Epidural hematoma	.....	72	72
J. P.	40	F	Compound comminuted skull fracture; cerebral laceration	.....	96	360
J. M.	?	M	Subdural hematoma	Cerebral infarction; lobar pneumonia	20	20
P. G.	?	M	Fracture of skull; epidural hematoma	Bronchopneumonia	96	96
E. F.	13	M	Subdural hematoma	Shock and respiratory failure	4	4
J. M.	35	M	Fracture of skull; subdural hematoma	Fracture of rib; hemothorax	7	7
F. R.	50	M	Fracture of skull; cerebral contusion	Multiple fractures of ribs; hemothorax; contusion of pancreas; hemoperitoneum	48	48

REPORT OF CASES

CASE 1.—M. H. was a 66-year-old white woman, who was admitted to Hahnemann Hospital on Aug. 20, 1949, in an emergency, soon after she fell down the steps in her home. The police stated that she was picked up unconscious and had vomited once. It was said that she had been drinking large quantities of beer and may have been inebriated. Examination revealed a left occipital scalp laceration, bleeding from the left ear, and multiple contusions of the left shoulder, trunk, and both lower extremities. Her skin was cold and clammy; pulse thready, and blood pressure 80/0. Neurological examination revealed no significant localizing signs. Her airway was cleared by repeated aspirations through the nose and mouth. She was given plasma transfusions and nasopharyngeal oxygen by mask and tube. Although the state of coma persisted and fluctuated in degree, the serious problem seemed to be a repeatedly obstructing airway. Consequently, on Aug. 22, a tracheostomy was done. In this way the trachea was continually aspirated, and oxygen was administered by catheter through the tracheostomy tube. On Aug. 23, at noon, 90 hours after she suffered her injury, the patient had a Jacksonian convulsion which originated with twitching of the right side of the face. Although these convulsions occurred every 30 minutes and became more violent, neurologically the only significant finding now was deepening coma, and lack of response to painful stimuli. At 9:00 p. m. exploratory trephination was done bilaterally, and a large subdural hematoma was discovered in the left parietal area.

TABLE 2.—*Twenty Patients with Tracheostomy Who Died*

Patient	Age	Sex	Head Injury	Complications	Tracheostomy Hr. After Adm.	Coma Hr.	Survival Hr.
R. P.	37	F	Laceration brain	Multiple fracture of ribs; hemothorax	Immediate	2,136	2,136
W. D.	53	M	Subdural hematoma	.....	8	4	12
M. T.	35	F	Skull fracture; subdural hematoma	.....	11	15	15
X.	35	M	Skull fracture; subdural hematoma; cerebral laceration	.....	11	51	51
A. K.	50	M	Skull fracture; cerebral contusion	.....	24	144	144
J. M.	32	M	Skull fracture; cerebral contusion	Multiple fractures of ribs; fractured mandible; fractured humerus	Immediate	2	2
E. B.	50	M	Diffuse craniocerebral	.....	Immediate	¼	¼
H. F.	35	F	Compound skull fracture; subdural hematoma; cerebral laceration	Fracture of rib; hemothorax; fracture of arm and leg	Immediate	18	18
E. W.	29	M	Skull fracture; laceration midbrain	.....	Immediate	20	20
F. U.	65	M	Subdural hematoma; cerebral contusion	.....	7	12½	12½
A. H.	37	M	Subdural hematoma	.....	4	1	120
S. M.	50	M	Cerebral contusion	.....	168	528	528
G. D.	52	M	Subdural hygroma	Bronchopneumonia	168	192	192
J. L.	45	M	Subdural hematoma; cerebral contusion	.....	72	96	96
D. K.	42	F	Subdural hematoma	Rheumatic heart disease; congestive heart failure; thrombophlebitis	140	48	144
J. D.	65	M	Multiple fracture of skull; cerebral contusion	Friedländer's meningitis	120	240	240
C. H.	40	M	Skull fracture; subdural hematoma, cerebral contusion	Meningitis	120	120	120
F. S.	60	F	Depressed skull fracture; cerebral contusion	Fractured pelvis; multiple rib fractures; hemothorax; atelectasis; pulmonary abscesses; fracture of femur	16	33	33
T. T.	51	M	Compound comminuted skull fracture; cerebral laceration	.....	Immediate	2	2
B. W.	39	F	Skull fracture; cerebral laceration	Fractured metatarsals	Immediate	2½	2½

TABLE 3.—*Six Patients with Tracheostomy Who Lived*

Patient	Age	Sex	Head Injury	Complications	Tracheostomy, Hr. After Adm.	Coma, Hr.	Condition on Discharge
M. S.	13	F	Skull fracture; epidural hemorrhage	.....	144	1,704	Discharged decerebrate; now ambulatory
B. B.	30	M	Skull fracture, compound; cerebral contusion	.....	48	0	Ambulatory
M. H.	66	F	Subdural hematoma	.....	48	528	Ambulatory
W. C.	60	M	Skull fracture, compound, comminuted; cerebral laceration	Diabetes mellitus	Immediate	Momentarily	Ambulatory
A. G.	63	M	Skull fracture; cerebral contusion	Fractured mandible	18	96	Ambulatory
K. G.	6	M	Cerebral contusion	.....	Immediate	24	Ambulatory

This was evacuated. Postoperatively the patient entered a very stormy course. She required constant and special attention to her airway and maintenance of her fluid, electrolyte, and nutritional balance. Fecal and urinary incontinence and bed sores were great nursing problems. She was given sodium sulfadiazine intravenously and penicillin by intramuscular injection. She was also given intravenous injections of glucose, electrolytes, and protein hydrolysates (Amigen), and blood transfusions. A Foley catheter was inserted, and accurate intake and output record was kept. She was given daily enemas to control incontinence and prevent fecal impaction. Eventually she was fed a high-protein and high-vitamin mixture by gastric tube. On Sept. 3 for the first time the patient seemed to be improved. On Sept. 4 and 5, several episodes of tracheal obstruction almost caused her death. However, these were controlled by better care and attention to the tracheostomy tube. After Sept. 7, she showed steady improvement. On Sept. 6 she was talking; on Sept. 24 she was walking; on Oct. 4 she was discharged from the hospital, to be followed in the neurosurgical follow-up clinic.

This patient suffered severe trauma to her central nervous system, which left her comatose for 22 days. Throughout this whole time, it was necessary to provide means for sustenance and maintenance of body functions. Not the least important of these factors was maintenance of a patent airway. Initially, endotracheal suction by catheter was attempted; however this proved inefficient, and consequently within 48 hours tracheostomy was instituted. Thereafter, constant diligent care was given to the patient's tracheobronchial toilet. We feel this played a major role in her eventual recovery.

Case 2.—M. S. was a 13-year-old white girl. The patient was admitted to Hahnemann Hospital in a semicomatose state five hours after being hit by a truck. Her temperature was 101.6; pulse 104; respiration 36; blood pressure 124/60. Examination revealed response to painful stimuli, bleeding from the nose and left ear, a dilated left pupil, and involuntary movements of all four extremities. The following day her sensorium cleared sufficiently for her to respond to questioning, but clear cerebrospinal fluid began to drain from her right nostril. Her condition on the third hospital day was unchanged. During this time her tracheobronchial tree was kept clear by periodic aspiration via a soft catheter. Skull x-rays disclosed two linear fractures of the left temporoparietal region. On the fourth hospital day, following cessation of spinal fluid drainage, there was a sudden rise in pulse pressure and a drop in pulse rate, and she became unresponsive to all stimuli. Exploratory trephination was made, and a large left epidural clot was evacuated. Her condition improved postoperatively; she was still comatose, but now responsive to painful stimuli. Because of the failure of endotracheal suction to maintain an unobstructed respiratory tract, a tracheostomy was done. Following this there was marked improvement and ease of respiratory effort. Progressively generalized spasticity developed, and she was discharged two months after admission in a decerebrate state. One month after discharge she improved to the point that there were no paralyses other than a right lower facial weakness; reflexes were equal and active, and coordination and sensation were within normal limits. She was grossly overweight; her left eye was blind, and a right temporal hemamopsia existed. Her hearing was good, and, since she was originally left-handed, she was able to write as well as ever. Although she was irritable, she cooperated nicely.

From the outset, extreme care was given to this patient's respiratory tract. When her initial voluntary efforts, assisted by endotracheal suction, were no longer effective, tracheostomy was instituted. We feel that the use of tracheostomy in this instance prevented a respiratory disaster.

Case 3.—W. C. was a 50-year-old Negro. He was admitted to the hospital in deep coma and shock after being struck by a trolley car. Physical examination showed his pulse was 80, respiration 20, and blood pressure 90/60. There was a compound, depressed fracture of the midfrontal area of the skull, with brain tissue extruding through the wound. He was bleeding from the nose and mouth. Neurological examination revealed nothing significant on admission. Shock therapy was instituted. A tracheostomy was done immediately because of marked respiratory difficulty and cyanosis. Following stabilization, he was taken to the operating room

for debridement of the wound and elevation of the depressed skull segment. Postoperatively, despite constant attention to the tracheostomy, bilateral basilar pneumonitis developed. This was successfully controlled by use of antibiotics and maintenance of a clear respiratory tract by periodic aspirations. In the course of routine laboratory studies, the patient was found to have diabetes mellitus and was treated accordingly. Through careful attention to fluid, electrolyte, nutritional, and insulin requirements, plus vigorous therapy directed against respiratory complications, the patient was thereafter able to make an uneventful recovery and he was discharged as ambulatory two months later.

In this case tracheostomy had twofold beneficial effects: initially, to relieve respiratory obstruction from retained secretions; and secondly, to provide an easy means of removing secretions and debris postoperatively from the tracheobronchial tree, thereby increasing the efficiency of the antibiotics used in the treatment of the patient's complicating pneumonitis.

COMMENT

Tracheostomy is being recognized as good therapy in the prevention of pulmonary complications in postoperative and severely debilitated patients.[6] In this

TABLE 4.—*Mortality of Acute Head Injury*

Type of Injury	No. of Cases	Mortality Rate, %
Acute head injury, total	1,000	7.4
Acute head injury without cerebral involvement	430	0.0
Acute head injury with cerebral involvement	570	13.0
Cerebral injury with skull fracture	203	26.1
Cerebral injury without skull fracture	367	5.7
Acute head injury; complicating rib fracture	40	35.0
Acute head injury; tracheostomy	20	60.0

respect, particular care of the neurosurgical patient is needed, since additional factors are present as a result of the cerebral injury itself[7]; i. e., decreased gag reflex, obstruction by relaxed pharyngeal musculature, aspiration of food, liquid, and saliva into the lungs, and the tendency for secretions to accumulate in the tracheobronchial tree. The occurrence of concomitant chest injuries among patients suffering from head trauma further increases the mortality rate (Table 4). Tracheostomy has been shown to have definite therapeutic effects in this group[8]: a mechanical cleansing of the airway by easy removal of excessive fluids or blood from the tracheobronchial tree, as well as relief of laryngeal obstruction from edema, bleeding, or faulty function of the vocal cords; and a physiological decrease in the amount of dead space in the respiratory tract, and a diminished resistance to breathing. Furthermore, tracheostomy has the advantages of being a well-tolerated, simple, and single procedure. It is direct and definitive. Less experienced ward

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help can take over aspiration and management of the oxygen catheter; and alcoholic, intractable, and severely injured patients are most easily managed in this manner.[9]

If there is any doubt as to the patency of the airway, it is best to do a tracheostomy. Certainly, a patient with manifest respiratory embarrassment demands tracheostomy, as well as any patient who has been comatose more than 24 hours. In this latter group great amounts of "hidden" bronchial and alveolar secretions may be raised by proper aspiration, even if no clinical signs of respiratory distress are evident.[10] These patients require constant vigilance, scrupulous care, frequent turning, and careful aspiration, with short periods of suction, in addition to the routine administration of oxygen, antibiotics, parenteral fluids, and alimentation, as indicated for each patient.

SUMMARY AND CONCLUSION

The pathophysiology of respiratory obstruction in acute head injury is discussed.

The methods of maintaining a patent airway are enumerated and evaluated.

Case reports and data are presented to illustrate the clinical difficulties of this problem.

Tracheostomy is the most effective measure in the management of the airway in acute head injury.

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ONE-STAGE TOTAL COLECTOMY INCLUDING ABDOMINOPERINEAL RESECTION WITH PRIMARY ILEOSTOMY

Surgical Treatment of Chronic Ulcerative Colitis and Familial Polyposis

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GENERAL agreement has been reached in most groups concerning the need for surgical intervention in the management of about 10 to 20% of cases with chronic ulcerative colitis and in 100% of cases with familial polyposis.[1] There is no controversy concerning the need of colectomy as soon as the diagnosis is established in those patients with polyposis, because statistical analysis has shown the high incidence of malignancy which exists or develops in this disease.[2]

Eventually in all patients with this disease, cancer will develop,[1e] and any procrastination on the part of the patient, physician, and/or surgeon may result in the loss of the one chance the patient may have for cure.

In chronic ulcerative colitis the need for surgery is dependent upon several factors. Most of the patients with this condition are a medical problem and are referred for surgical management under specific indications. These indications are generally agreed upon: protracted disease with irreversible anatomic and functional changes; chronic sepsis in the colon in which there may be long periods of morbidity and incapacitation requiring continuous active medical measures; financial difficulties resulting from the need for constant treatment; chronic relapsing and remitting form of the disease; obstruction, perforation, or impending perforation, abscess, and anorectal complications, such as painful intractable fissures or fistulas; arthritic and skin changes as a result of the disease; development of pseudopolyps; recurrent bleeding or hemorrhage from the colon; development of adenomatous hyperplasia and cancer, and segmental involvement. The latter two complications have stimulated a great deal of interest recently.

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It is apparent from recent reports in the literature that the incidence of carcinoma of the colon is much higher in patients with chronic ulcerative colitis than the incidence of cancer of the colon in the general population.[3] The results of treatment of carcinoma developing in cases of ulcerative colitis have been particularly poor as compared with the results of treatment of the usual type of carcinoma of the colon.[1d] It also has been shown that the incidence of carcinoma in patients with chronic ulcerative colitis over 10 years' duration is much higher than in those who have had the disease less than 5 years.[4]

It is not the purpose of this report to imply that all patients with ulcerative colitis should be subjected to a colectomy. However, those who meet the criteria as outlined above should be managed surgically. It has been the policy, and still is in many centers, that surgical treatment consists of an ileostomy, as a preliminary or only operation in a great number of cases, or of an ileostomy and subsequent partial or total colectomy in some cases. Occasionally, a segmental resection of the colon is performed in the few patients who are fortunate to have only a segmental type of colitis.[5] Surprisingly, the mortality rates for partial or total colectomy are much lower than those for ileostomy alone. This, however, may be explained because in the majority of instances the ileostomy is performed as a last resort in the fulminating stages of the disease and the patient is referred to the surgeon too late. Preliminary ileostomy in many of this group is necessary in order to improve the general health and nutrition so that the patient will be a safer candidate for subsequent colectomy. Colectomy, subtotal or total, is generally performed as a two- to three-stage procedure. However, a single-stage total colectomy with or without a preliminary ileostomy has been and can be performed with a certain degree of safety, provided careful preoperative, operative, and postoperative management of the patient is rigidly observed.[6] The multiple-stage technique increases the risk and frequently results in a higher over-all mortality.[7] It is our opinion, too, that the late results in subtotal or total colectomy are more favorable in the majority of patients meeting the criteria discussed above than ileostomy alone. This, however, is not to imply that all patients requiring surgical treatment should be subjected to a colectomy.

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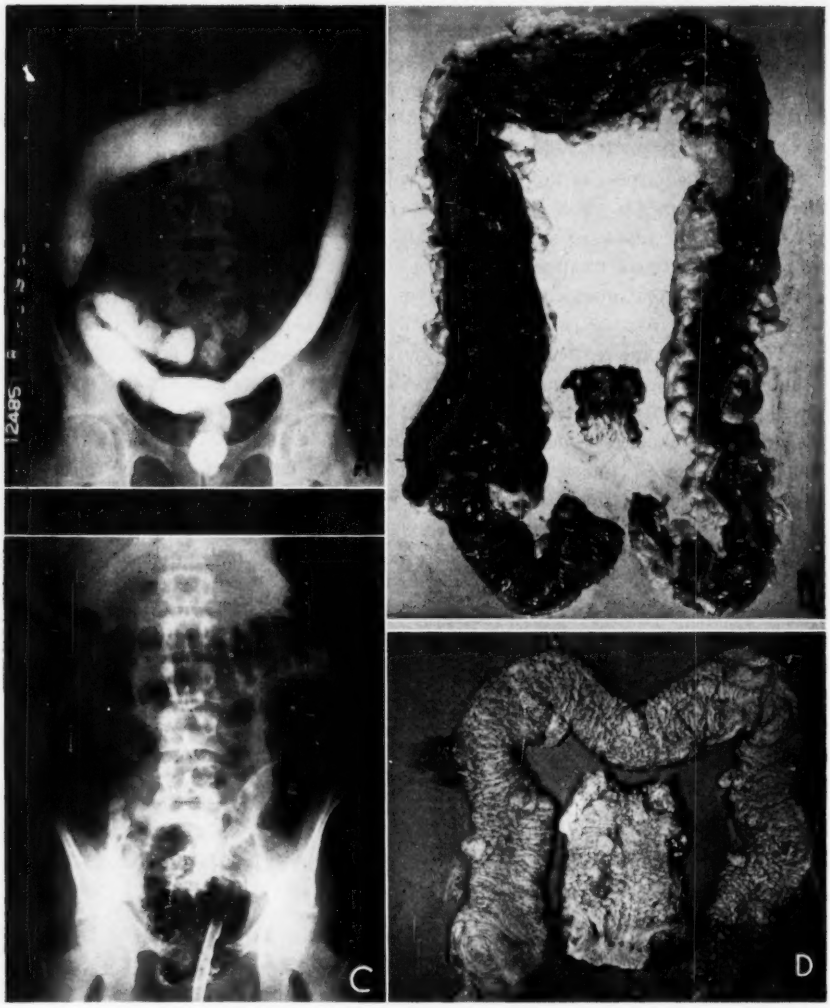

Fig. 1.—*A*, barium enema revealing advanced chronic ulcerative colitis. Colon is foreshortened and tubular with fewer haustral and mucosal markings. *B*, portion of terminal ileum and entire colon, including rectum and anus, is shown. Mucosa is velvety and thickened; dark areas represent ulceration. Sigmoid, rectum, and anal canal are rigid and narrowed. *C*, air-contrast enema revealing polypoid changes in the colon in a case of familial polyposis. *D*, entire colon, including rectum and anal canal, is a mass of polyps of all sizes. Dark areas on outer margins of the ascending and descending colon represent large polyps which reveal adenocarcinoma.

ONE-STAGE TOTAL COLECTOMY

Since July, 1950, we have performed a one-stage total colectomy (including removal of the rectum and anus) with or without preliminary ileostomy in nine patients, and in two we performed a subtotal colectomy with an ileorectosigmoidostomy. These were all consecutive cases in which the patients were referred for surgical treatment of ulcerative colitis or familial polyposis during this period of time. All of the patients with chronic ulcerative colitis had far-advanced irreversible changes in the colon, with long periods of disability, poor nutritional state, and in some, systemic manifestations of their disease. These patients had failed to respond to prolonged courses of medical management.

In two cases a preliminary ileostomy was performed. This was necessary because these patients were operated on late and in an acute septic stage in their disease. However, after this procedure they improved considerably, so that at a later date a one-stage total colectomy could be performed with safety.

The pathological changes in the colon in the nine patients presented were so extensive and advanced that a total colectomy, including the anal outlet and canal, was necessary (Fig. 1). In the remaining two cases the pathology was limited primarily to the terminal ileum and colon down to the sigmoid. Here we thought it would be safe to preserve the distal segment; consequently we performed an ileorectosigmoidostomy and closely observed the remaining colon and rectum by periodic follow-up proctoscopic examinations. In one of these patients who had familial polyposis, recurrent carcinoma subsequently developed in the region of the anastomosis, and an abdominoperineal resection and permanent ileostomy were performed.

AGE INCIDENCE AND TYPES OF DISEASES TREATED

In this series there were 10 patients, with an over-all average age of 34.2 years. The ages ranged from 24 to 57 years. The average age for the patients with ulcerative colitis was 37 years, the youngest 24, and the oldest 57, whereas in the patients with familial polyposis, the average age was 32 years, the youngest 27, and the oldest 40.

Four patients in this series had extensive familial polyposis, including the anal canal and the rectum (Fig. 1*C* and *D*). These changes were so marked and advanced that local observation and fulguration through a proctoscope were both impossible and unsafe. In three (75%) of the patients an associated adenocarcinoma was found. One patient had two lesions, one in the descending and the other in the ascending colon. A preliminary ileostomy was not performed in any of these cases.

Seven patients of this series had advanced ulcerative colitis (Fig. 1*A* and *B*); none of this group had an associated carcinoma.

All operations were performed with use of endotracheal anesthesia. Careful attention was given to proper protein, fluid, and electrolyte replacement preoperatively. Blood transfusions were given in amounts necessary to restore the blood count and the blood volume to normal levels.

INCISIONS

In eight cases a transverse elliptical infraumbilical incision was employed; in two, a transverse elliptical supraumbilical incision was utilized, and in one, a left vertical paramedian incision was made. It is our opinion that the most anatomical and physiologically sound incision and one which provides adequate exposure is the

infraumbilical incision (Fig. 2). This incision is placed several inches below the umbilicus, being carried through the skin and superficial fascia in a transverse elliptical direction. The anterior and posterior rectus sheath layers are, likewise, divided transversely, and both rectus abdominis muscles are transected. The deep inferior epigastric vessels are ligated and divided, and the peritoneum is opened in the same direction. This provides ample and complete exposure of all the abdomen, particularly the lower two-thirds and the pelvis.

The colectomy can be carried out rather rapidly from right to left and the procedure terminated at any point if the patient's condition demands it. The colon is mobilized on the left as for an abdominoperineal resection. However, in those

Fig. 2.—Photograph of abdomen of patient who had a one-stage total colectomy, including abdominoperineal portion and ileostomy, taken one year postoperatively. Transverse infraumbilical incision is seen, and ileostomy is functioning well through a modified McBurney-type incision. Circular ring about the ileostomy is the imprint made by the adhesive diaphragm of the Duval-type ileostomy bag.

patients in whom a malignant lesion does not exist in the sigmoid, rectum, or anal segments, the dissection in these areas is kept close to the bowel wall in order to minimize the damage to the autonomic nerve supply to the bladder, prostate, and seminal vesicles. This is important in preventing bladder dysfunction and/or impotency. The rectum is divided near the levator ani muscles, and the anal canal and rectum are removed from a perineal approach. Again, the dissection is carried out in close proximity to the bowel wall. The perineal wound is managed with a perineal pack.

The raw surfaces on the posterior body wall resulting from the colon resection are not reperitonealized. A small bowel obstruction did not result in any of our cases

because of this. Wound closure is accomplished with use of nonabsorbable surgical sutures, usually silk. The peritoneum is closed with interrupted 000 silk; the anterior and posterior rectus sheaths, with 00 silk.

It is our policy to establish the permanent ileostomy through a modified McBurney incision, which is placed a little higher than McBurney's point. The skin incision is placed in a transverse direction, in the direction of normal lines of stress and strain (Fig. 2). The three muscles of the anterior abdominal wall are split in the direction of their fibers—this type of incision aids in providing both support to the ileostomy and a sphincteric action to the ostium. With the placement of the ileostomy at this point, there is no interference with the proper fitting of a Duval or Rutzen-type ileostomy bag. It is in an area of the abdomen where retraction of the wound or of the abdomen does not occur and is far enough away from the abdominal incision not to be a hinderance to wound healing. The ileum is anchored to the anterior abdominal wall at its mesenteric border. In none of these instances and in a series of 30 patients with this type of ileostomy, no retraction, gangrene, or fistula developed. In two patients, prolapse of the ileostomy occurred, and in one stenosis of the stoma resulted. These three complications were managed without too much difficulty.

RESULTS

All patients were ambulated on the first postoperative day without increasing the morbidity or the wound-complication rates. The only complications which developed were one retroperitoneal abscess and a homologous serum hepatitis. In order to overcome bladder dysfunction following surgery, a Foley catheter was maintained for bladder drainage for an average of 10 days. None of these patients experienced chest complications or thrombophlebitis.

All wounds healed per priman, and on repeated follow-up studies there were no cases of postoperative hernias.

During the first postoperative week, particularly in those patients in whom ileostomy was performed at the time of colectomy, careful and rigid observations and laboratory studies were carried out in order to replace adequately the potassium, sodium, and chloride losses which may result in great quantities during this critical period. Also, attention to proper and adequate fluid and blood replacement to maintain the normal circulating volume and the normal intracellular and extracellular water and electrolyte balances was rigidly practiced. The average amount of blood given during the operative procedure was 1,750 cc.

There were no operative or postoperative deaths in this series. In fact, the patients tolerated the procedure and the postoperative period very well.

One patient with crippling arthritis as a result of ulcerative colitis experienced dramatic symptomatic improvement, although joint deformities persisted because of irreversible pathological joint changes.

All patients, especially those with ulcerative colitis and the one patient with polyposis without cancer, showed immediate and progressive gain in weight and marked improvement in general health and well-being.

All married patients seen on follow-up examinations experienced essentially normal sexual function. There were no cases of impotency or failure of erection. Two patients complained of lack of sexual libido despite normal erection and ejaculation. Our consulting urologist felt these complaints were on a psychogenic basis.

Most of the patients were fitted with and had good results with a Duval-type ileostomy bag.

SUMMARY AND CONCLUSIONS

In 10 to 20% of patients with chronic ulcerative colitis and in 100% of patients with familial polyposis surgical treatment is necessary. In both groups the general trend is to perform subtotal or total colectomy by a multiple-staged procedure.

In nine consecutive cases, in which six of the patients had far-advanced ulcerative colitis and three had familial polyposis, a one-stage total colectomy (including the abdominoperineal portion) was performed. In two of these patients a preliminary ileostomy had been done previously, and in the remaining seven, the ileostomy was established at the time of colectomy. In two other patients, one with polyposis and one with advanced ulcerative colitis, a one-stage colectomy with an ileorectosigmoidostomy was performed.

There were no deaths in this series, and the morbidity was minimal. The operation was accomplished through a transverse elliptical supraumbilical or infraumbilical incision without difficulty and without wound complications, including no cases of postoperative hernia.

Careful attention to preoperative, operative, and postoperative management, especially to proper protein, fluid, and electrolyte balance and replacement; and adequate whole blood replacement, particularly during and immediately after surgery to maintain normal circulating volume, are important essentials in these patients and will permit the performance of a one-stage procedure with a certain degree of safety.

By careful dissection close to the bowel wall in performing the abdominoperineal portion of this operation, damage to the autonomic nerve supply of the bladder and associated structures will be minimized, thereby preserving normal bladder and sexual functions postoperatively.

It is our opinion at this time that many patients with these two diseases requiring colectomy could withstand a one-stage total colectomy with or without a preliminary ileostomy better than they could withstand a multiple-staged operation.

Case Reports

SEVERE BURN TREATED WITH CORTISONE AND WITHOUT SKIN GRAFTING

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IN THE following case report a new method of burn treatment without skin grafting is described. This method is believed very valuable because pain is quickly allayed, recovery prompt, and scarring minimized.

REPORT OF A CASE

On June 11, 1952, a housewife's dress caught fire while she was making supper, and the dress was half consumed before the flames were extinguished with a blanket. Medical care was started within 15 minutes of the accident. Morphine sulfate, ½ grain (30 mg.), was given intramuscularly, and 1½ lb. (0.7 kg.) of an ointment was applied to the burned area,[1] which included the entire upper left limb from fingertips to shoulder and over 60% of the left torso, anteriorly and posteriorly, and also the entire left buttock and one-half of the right buttock, one-third of right lower sacroiliac area, and the entire left thigh down to the knee joint. Penicillin, 600,000 units, was given intramuscularly after the dressing was completed and this treatment repeated daily for the next two weeks, when 1 ampule of combined penicillin (300,000) and streptomycin (1 gm.) daily was started. The blood pressure was 120/80 and the pulse rate 85; the patient was so comfortable she refused hospitalization.

On the first day following the accident, on removal of the dressing, 75% of the burned area was found to be of second- and third-degree intensity and 25% of first degree. Gentle débridement, removing all loose dead skin and blisters, was done. On the second day the volar surface of the entire left limb was blackened, as well as the left breast, abdomen, back, and left buttock.

Because of the great area burned, daily dressings were then made in three successive sections as follows: first day, entire left upper limb; second day, torso; third day, buttock and thigh. Daily débridement both by mechanical methods and also with repeated applications of tepid wet towels, thickly soaped, were applied from 30 minutes' up to 1 hour's duration. Supportive measures of oral forced fluid (5,000 to 6,000 cc. a day) codeine, acetylsalicylic acid, ascorbic acid, vitamin B_1, nicotinamide, and phenobarbital were instituted on second day. On the fourth day the patient began to menstruate and became extremely emotional and difficult to control. Menstruation, unfortunately, continued for 17 days. The administration of cortisone (100 mg. initially and decreased by 25 mg. daily) was started on the ninth day.[2] For first two weeks the temperature never rose to over 101 F. Owing partly to the protracted menstruation as well as to the burn itself, the hemoglobin concentration fell to 37% of normal. Over violent protestations of the patient, hospitalization was insisted upon and carried out.

Two pints of blood was given within 12 hours of hospitalization, after which cyanosis disappeared and the hemoglobin level rose to 50%. The temperature began to spike to 103 and 104 F. Daily dressings and débridement were now made, a layer each of two different ointments being used (the first for anesthetic effect, to help combat shock, and the second for bacteriostatic effect, to control infection). Use of penicillin was discontinued, and one ampule of combined penicillin and streptomycin daily was started. Large amounts of food, consisting of milk and orange juice, with vitamins, and a high-protein, high-vitamin diet were given during the entire

1. The principle of local ointment application is first anesthetic, second antibacterial, and third antigranulation or proepithelization.

2. Use of cortisone prevents granulation and scar formation and allows epithelization. This minimizes or averts the necessity for plastic surgery in many cases. Suitable ointments are selected for their anesthetic, antibacterial, and proepithelization qualities.

hospital stay. Cortisone, 100 mg. daily, was given on the second day of hospitalization when the temperature was 104 F. The next day it went down to 100 F. Cortisone was discontinued after six days. At the end of the second week, after the temperature rose to 105.6 F., it was decided to stop all antibiotic therapy and start cortisone again on the theory that the temperature was now primarily due to granular tissue formation and not to infection. This theory was further strengthened by the fact that after two days of treatment with oxytetracycline (Terramycin) the temperature still rose to 104 F., and even though the antibiotics were then discontinued, with the administration of cortisone alone (100 mg. daily) the temperature returned to normal in 24 hours. Cortisone was then given for five days, during which time there was some edema of the ankles. A curious side light to the administration of cortisone was the occurrence of a definite euphoria in the first 24 hours of each course, and during the second course the patient acquired from a fellow patient alongside her a foreign accent, which disappeared in two days.

After a third transfusion the hemoglobin value rose to 62% of normal. Three daily injections of vitamin B complex and Reticulogen (brand of purified liver extract) also were given during first three weeks of hospital stay. After a fourth transfusion the hemoglobin value rose to 74%, and transfusions were discontinued. Daily dressings, as described, with a variety of local medicaments probably had no specific affect. The wounds healed with concentric epithelization. The cortisone may have retarded granulation (scar) tissue formation. Meticulous cleansing of skin edges from adhesive tape probably enhanced epithelization.

On some days while dressing the wound, new skin formed to as much as a 2-in. (5 cm.) concentric growth, which closely resembled newly grafted skin. On each successive day dressings became smaller, until all the second and third degree areas were covered by normal or slightly mottled smooth skin.

SUMMARY

An extensive flame burn of first, second, and third degree intensity, involving about 25% of the body surface area, was treated, with neglegible scar formation and with complete recovery of motor function without any plastic or restorative surgical procedure. The entire time required for healing was slightly less than 11 weeks.

Treatment included early and immediate relief of pain, antibiotic medication to combat infection, blood transfusions to combat hemoglobin depletion, daily dressings and daily débridement to minimize scar formation, cortisone therapy, and supportive measures of large doses of ascorbic acid, micotinamide and other vitamins, milk, and high-protein diet. Finally psychotherapy was also used to allay emotional tension.

This case illustrates the fact that deep burns may heal without skin grafts when islands of hair follicles and sweat glands remain in areas of third degree involvement. It was from these islands that regeneration occurred.

IDIOPATHIC DILATATION OF THE COMMON BILE DUCT

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THE REMARKABLE character and extreme rarity of idiopathic dilatation of the common bile duct (congenital choledochal cyst) render it a lesion of such interest as to justify the report of a single case.

Shallow and Eger,[1] in 1943, reviewed the subject and were able to collect only 175 well-authenticated cases from world literature. Their material was well organized and dealt with all phases of the condition so thoroughly that detailed discussion of the clinical features of the condition in this paper would be repetitious. Information gained from their work and additional isolated case reports and small series of cases since that time [2] have helped to clarify the diagnosis and treatment of this lesion. Of considerable historical interest but not brought out in their paper was the fact that the first recorded successfully treated case was reported by Williams and Smithwick [3] in 1929. The patient was a 5-year-old child who had had the initial idiopathic dilatation of the common duct treated by the creation of a biliary fistula. A successful outcome followed Dr. Williams' transplantation of this cutaneous fistula into the duodenum. The operation was done in 1913.

In discussing the unusual features of idiopathic dilatation of the common duct, its rarity must be stressed. Smith,[4] at the Presbyterian Hospital in New York, was able to find only two cases in 757,000 admissions. The high mortality associated with the lesion is directly related to this rarity, since the application of adequate corrective measures is dependent upon recognition of the nature of the pathologic change. Although successful outcomes have followed other procedures, by far the lowest mortality and morbidity rates have followed the anastomosis of the cyst to the intestine, preferably the duodenum. This point is emphasized and well substantiated in the series presented by Ladd and Gross.[5]

The etiology of the cyst formation is obscure. The dramatic appearance of the lesion, usually limited to the common duct, is startling. The capacity of the cyst

From the Department of Surgery, Straub Clinic.

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has often been reported in excess of 1,000 cc. It is agreed that the basic pathology is congenital, but why this local dilatation should occur without actual mechanical blockage is a mystery. Valves, fibrosis, irregularities, and many other local lesions at or near the ampulla have been described but have not been found consistently. These are all late findings and may be representative of gross changes due to the increasing size of the cyst, rather than primary etiologic factors. It is interesting and an unexplained fact that females are four times as often affected as males. It is our opinion, shared by others, that the condition is probably closely allied with Hirschsprung's disease, achalasia, and other disorders of smooth muscle.

The symptomatology and clinical course of the patient suffering from idiopathic dilatation of the common duct are often deceiving. Symptoms may in fact be lacking until the dilatation has reached huge proportions. A triad of pain, right upper quadrant mass, and jaundice has been described and is presumed to be pathognomonic when seen in children. However, this same triad may be seen in other conditions of the right upper quadrant and accounts somewhat for the fact that a correct preoperative diagnosis is infrequently made. A choledochal cyst is primarily a disease of childhood and early adult life, although cases in patients of advanced age have been reported. If we are aware of the condition and are presented with a child with pain in the abdomen, fever, often chills, fluctuating jaundice, and a palpable mass in the right upper quadrant, the diagnosis of choledochal cyst should be made. In most of the cases diagnosed preoperatively, the patient had been under observation for a considerable period and presented a mass that fluctuated in size in the right upper quadrant. As more cases are reported and the condition receives more notice, its presence should be suspected more and more frequently preoperatively.

The mortality with which this condition has been accompanied in the past is a direct challenge to pediatricians, internists, and surgeons alike. The mortality rate has fallen from 83% in 1927 to 20% at the present time. Even 20%, with present surgical knowledge and technique, is excessive for any nonmalignant and readily accessible lesion. Diagnosis before permanent liver damage has occurred, in addition to recognition and proper surgical procedures on the operating table, will further lower the mortality rate. In the case to be reported the diagnosis was made tentatively by one of us (Cherry) preoperatively.

REPORT OF A CASE

G. F., a Japanese boy, age 14, was seen as an out-patient in the Straub Clinic on April 10, 1950, with a chief complaint of pain in the epigastrium, slight fever, and malaise.

Examination at the time of this visit revealed an icteric sclera and tenderness in the region of the right and left lobes of the liver. A medical consultant felt at that time that he was suffering from infectious hepatitis.

The patient was hospitalized, and liver function studies were made, but the results were equivocal though suggestive of an obstructive type of jaundice. When the studies were completed, the patient was released from the hospital and was followed as an out-patient for a period of six weeks, during which time his jaundice fluctuated in degree and there was a marked variation of values in the laboratory studies, which were repeated frequently.

He was admitted to Queen's Hospital on May 29, 1950, eight weeks after the onset of his original illness. At that time his symptoms were severer, and his jaundice was more pronounced than it had been at any previous time. The van den Bergh test on this admission revealed a total of 28.4 mg. of bilirubin per 100 cc. of serum, with 20 mg. per 100 cc. direct and 8.4 mg. per

100 cc. indirect reaction. During this hospitalization, for the first time a mass was felt in the right upper quadrant, and during the next two days the mass increased rapidly in size. It was the opinion of one of us (Burgess) that we were dealing with a primary liver hepatoma, although, as previously stated, one of us (Cherry) felt that it was an idiopathic dilatation of the common duct.

The patient was prepared with transfusion of 500 cc. of blood and adequate vitamin K therapy and was operated upon on June 1, 1950. Under ether anesthesia, the peritoneal cavity was entered through a long right rectus incision, and exploration revealed a cystic mass, which appeared to be a huge dilated common duct (Fig. 1). The hepatic ducts were approximately 2 in. (5.08 cm.) in diameter, the cystic duct about 1 in. (2.54 cm.) in diameter, and the common

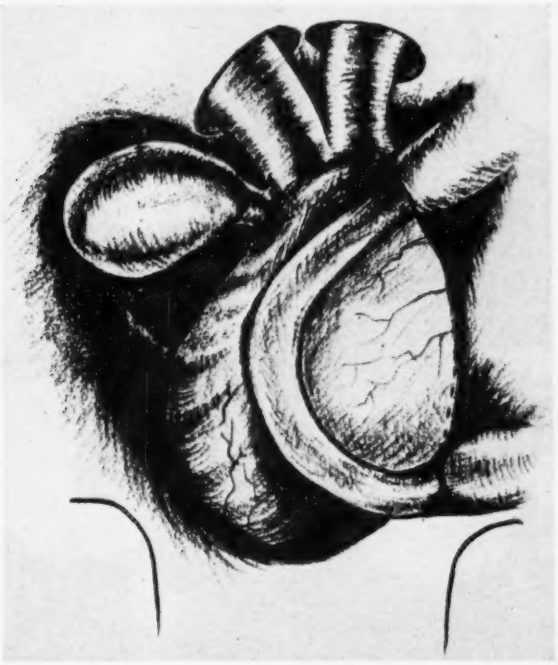

Fig. 1.—Drawing depicts the cyst as it appeared when it was exposed at the time of surgery. The hepatic ducts were tremendously enlarged but did not enter into the formation of the cyst. The gall bladder appeared to be a diverticulum arising from the lateral side of the proximal end of the cyst. The tubular structure stretched over the front of the huge cyst is the duodenum.

duct in its lowermost portion 4 to 5 in. (10.16 to 12.70 cm.) in diameter. The structure extended down into the true pelvis. The duodenum was drawn tightly across this tense cyst.

The cyst was aspirated in a suitable area that could later be used for anastomosing it to the duodenum, and 2,200 cc. of thin greenish bile was removed. This, of course, caused the cyst to collapse and facilitated the performance of a choledochocystoduodenostomy. The anastomosis, which was 2 in. (5.08 cm.) in length, was effected by using one row of continuous chromic 00 Atraumatic suture and one row of interrupted silk sutures. The suture line was reinforced with omental tabs. The patient received 500 cc. of blood during the operation and 500 cc. more after return to the ward: he withstood the operative procedure very well. There was no excessive oozing or any other technical difficulty during surgery. The incision was closed with interrupted 000 silk and retention sutures.

Convalescence was remarkably smooth and uneventful. Wangensteen suction was utilized for three days, after which time peristalsis and the passage of flatus announced the return of intestinal function. Clear liquids were then administered, which were tolerated well. The diet was rapidly increased, so that on discharge, eight days after admission, he was eating semisolid foods and having no discomfort of any kind. He has been followed at the Straub Clinic at regular intervals, and during the period from June 1, 1950, until July 28, 1952, seven different x-ray studies of the anastomosis have been performed. The illustrations demonstrate very well what

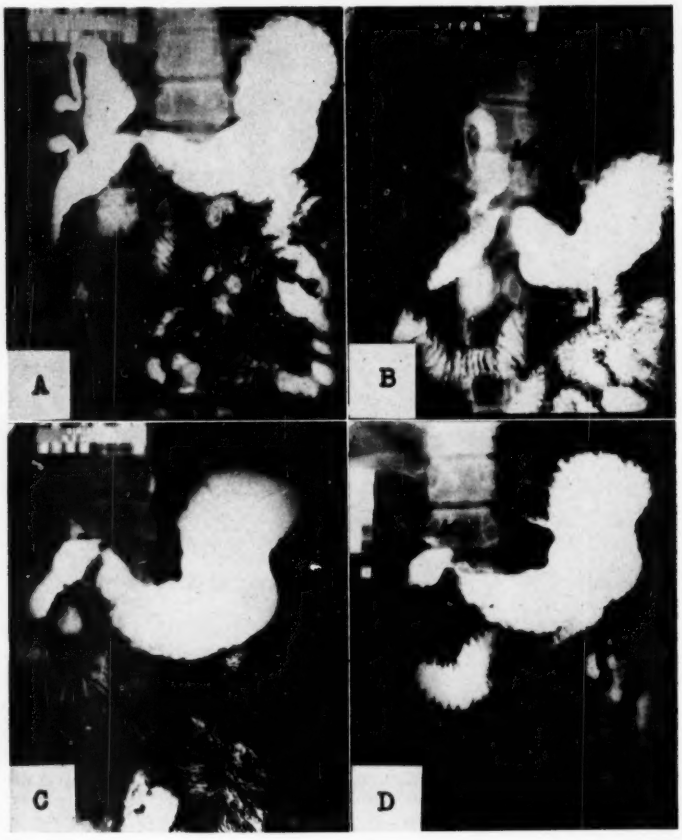

Fig. 2.—*A*, barium study of the duodenum six weeks after choledochoduodenostomy reveals filling of the common duct, both superior and inferomedial, to the duodenum. Marked decrease in the size of the common duct is revealed, but it is still a tremendous structure. *B*, similar study two and one-half months after surgery reveals further reduction in the size of the common duct. A saccular portion of the duct is still visible below and medial to the second portion of the duodenum. *C*, roentgenogram of the common duct outlined by barium six months postoperatively. No ill effects were observed following the introduction of barium into the common duct during these studies. *D*, repeat barium study two years following surgery demonstrates a remarkable reduction in the size of the common duct. It is thought that the appendiceal-like structure above and lateral to that portion of the duct indicated by the arrow may represent the gall bladder, though it could not be outlined during studies with gall bladder dye.

has happened to the huge dilated common duct (Fig. 2). In July, 1952, a repeat oral gall bladder dye study again failed to reveal any trace of a gall bladder.

SUMMARY

A case of idiopathic dilatation of the common duct has been presented. Although the early phase of the patient's illness was so suggestive of toxic hepatitis that surgical exploration was not considered, it is obivous that the patient's symptoms resulted from an idiopathic dilatation of the common duct. Finally, deepening jaundice and the development of a mass suggested the presence of a choledochal cyst. At surgery the findings were typical, and an anastomosis was performed between the cyst and the duodenum. It is anticipated that a permanent good result will ensue, although in June, 1952, the patient did have a mild attack of cholangitis with slight fever and barely perceptible jaundice, which persisted for about three days and then subsided. He has been in excellent health since.

The literature has been briefly reviewed, and special emphasis has been placed on the recognition of the condition at the time of surgery and the performance of what is at the present time considered the procedure of choice, choledocho-duodenostomy.

FOREIGN BODY IN THE RENAL PELVIS

Removal of Piece of Nephrostomy Tube with Nesbit Resectoscope

WALTER A. SCHLOSS, M.D.
AND
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NEWINGTON, CONN.

THE PRESENCE of a foreign body in the renal pelvis is not a common occurrence. In a recent complete review of the literature, Osmond [1] found reports of 34 cases of foreign bodies in the kidney or in the kidney pelvis and reported 4 additional cases. Another recent case was reported by Nelson and his associates,[2] of a bobby pin in the kidney pelvis.

An analysis of what was done in these 39 reported cases reveals the following:

Known cases with operation		29
Nephrectomy	10	
Pyelotomy	9	
Nephrotomy	4	
Duodenotomy	2	
Type of surgical approach not stated	2	
Laparotomy	1	
Abscess drained	1	
Refused surgery		1
Autopsy		1
Reports not available		8
Total known cases		39

In none of the cases in which the type of treatment was stated was the foreign body removed from the kidney or its pelvis without open operation. We are reporting a case in which a piece of nephrostomy tube was removed with the Nesbit resectoscope from the renal pelvis via a nephrostomy sinus.

REPORT OF A CASE

A 41-year-old white man had had multiple urologic complications of genitourinary tuberculosis. He had undergone a right nephrectomy and a left cutaneous ureterostomy. An abscess developed subsequently, which was drained; the left ureteral stump resected, and a left nephrostomy performed three years prior to the present admission. He then entered the hospital for a change of the nephrostomy tube. The previous tube, a two-wing Malecot, had fallen out, and his local physician had inserted a small (No. 18F.) straight Robinson catheter. This catheter

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1. Osmond, J. D.: Foreign Bodies in the Kidney: A Review of the Literature and Reports of 4 Additional Cases, Radiology **60**:375 (March) 1953.

2. Nelson, O. A., and others: A Bobby Pin in the Kidney Pelvis, J. Urol. **69**:618 (May) 1953.

was in place, but there was considerable leakage around it. A 22F. two-winged Malecot was inserted into the nephrostomy with some difficulty, since the tract had apparently become stenosed. This catheter did not drain properly, and it was decided to remove it at once and try to reinsert another. When it was pulled out, the distal half of the head of the catheter was missing (Fig. 1). No urine escaped from the nephrostomy opening. Several attempts were

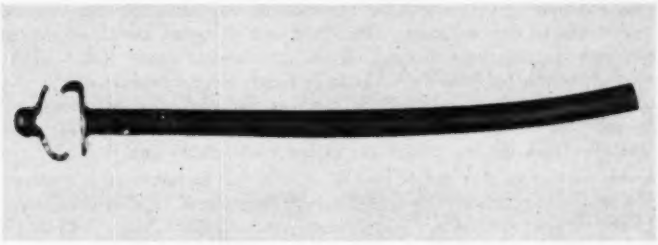

Fig. 1.—Photograph showing where break occurred in head of two-wing Malecot catheter. tip of which remained in renal pelvis.

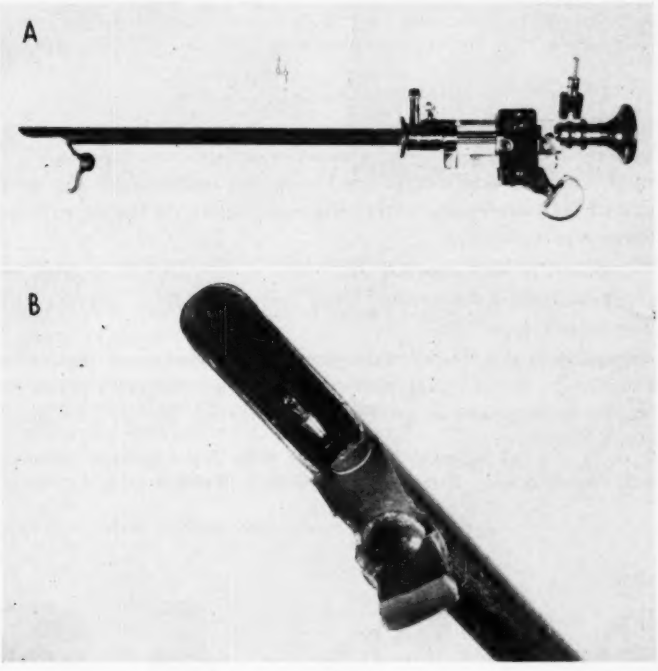

Fig. 2.—*A*, photograph showing how tip of Malecot catheter was grasped by electrotome loop of Nesbit resectoscope and withdrawn via nephrostomy sinus. *B*, close-up view showing catheter tip firmly engaged between loop and resectoscope sheath.

then made to recover the catheter tip by the use of a Kelly clamp, but each time it was grasped only a minute fragment of rubber could be recovered. Attempts were then made to grasp the catheter by using the panendoscope and foreign-body forceps, but again only a small fragment was recovered. Soon the entire piece disappeared from vision, and bleeding became somewhat

alarming. A new 22F. Malecot was inserted without too much difficulty, since the nephrostomy sinus had been dilated by the endoscopic procedures. Because of the foreign body in the renal pelvis and the bloody returns on irrigation, the patient was admitted.

Since the urine was strongly alkaline, the catheter was irrigated with 1% phosphoric acid. The nonprotein nitrogen was 31 mg. per 100cc. He was given antibiotics prophylactically and blood replacement for low hematocrit level.

When his condition stabilized and the nephrostomy tube drainage remained clear for 72 hours, he was taken to the operating room. With use of spinal anesthesia the renal pelvis was explored with the 24F. panendoscope via the nephrostomy sinus. The foreign body was seen but could not be grasped with the alligator or biopsy forceps because it kept moving away in the capacious renal pelvis. The visualizing lithotrite was next tried, but this too was unsuccessful, since the piece of catheter could not be grasped in the jaws. Aspiration with the Ellik evacuator was also tried, but this caused the patient considerable pain.

Because of the success that one of us (W. A. S.) had in removing a thermometer from the bladder with the resectoscope,[3] this procedure was employed. The nephrostomy tract was dilated to 28 F. with straight sounds. The Nesbit resectoscope (28 F.) was then introduced without difficulty, and with surprising ease the piece of nephrostomy tube was caught between the electrotome loop and the resectoscope sheath under perfect vision.

The resectoscope was then removed, holding the foreign body in place, which came out intact (Fig. 2).

A new Malecot nephrostomy tube was readily inserted, and the patient was returned to his room in good condition. He was discharged from the hospital 48 hours later.

SUMMARY AND CONCLUSIONS

A patient with a nephrostomy in a single remaining kidney was admitted to the hospital because the tip of a defective Malecot catheter had been lost in the renal pelvis during the removal of a catheter. The Nesbit resectoscope was used successfully to extract this foreign body from the renal pelvis via the nephrostomy sinus. Convalescence was uneventful.

In conclusion it is recommended that, prior to use, all rubber tubes and drains be carefully inspected for damage and weak points in order to prevent further accidents of this nature.

A simplified method is described, applicable in selected cases, for the removal of foreign bodies under direct vision from viscera such as the kidney pelvis or bladder, with use of the Nesbit resectoscope, thereby eliminating the need for open surgery.

3. Schloss, W. A., and Solomkin, M.: Foreign Body in the Bladder: Removal of Thermometer with Stern-McCarthy Resectoscope, J. A. M. A. **143**:804 (July 1) 1950.

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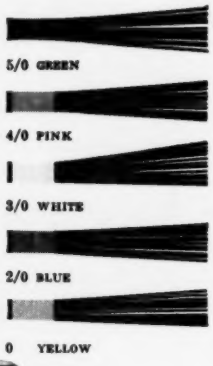

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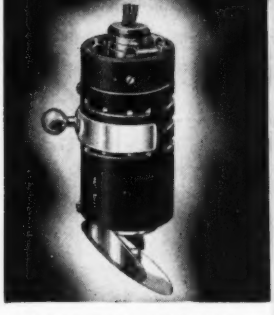

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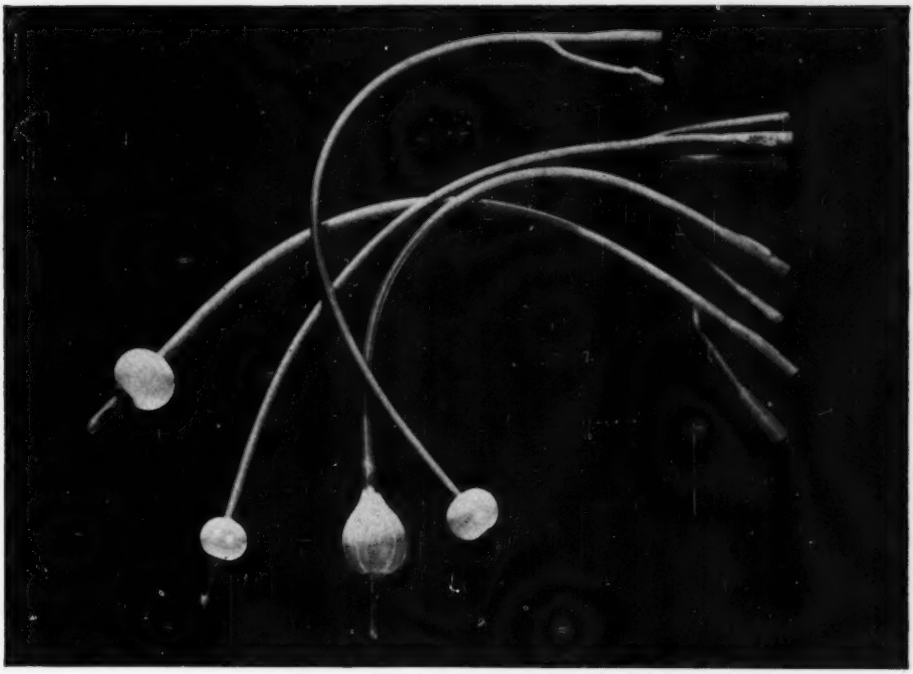

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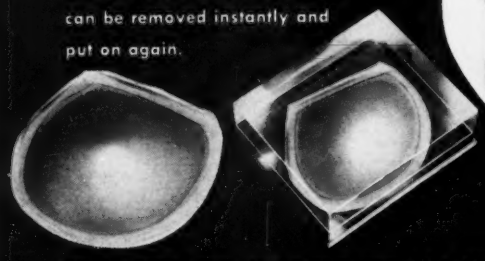

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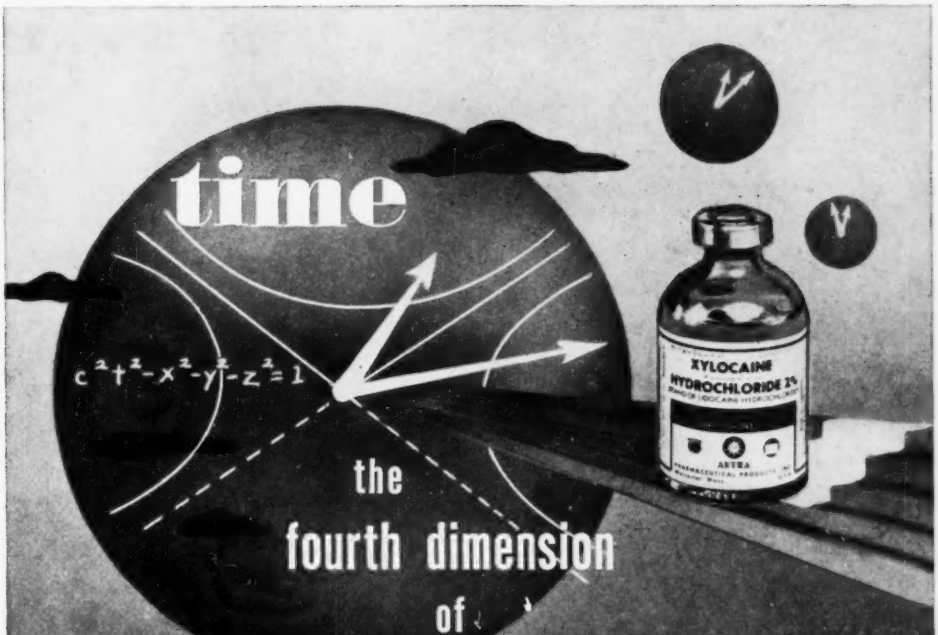

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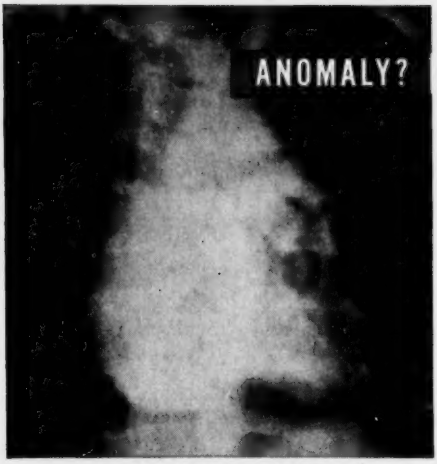

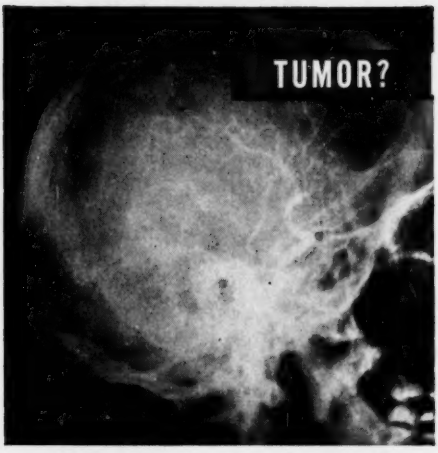

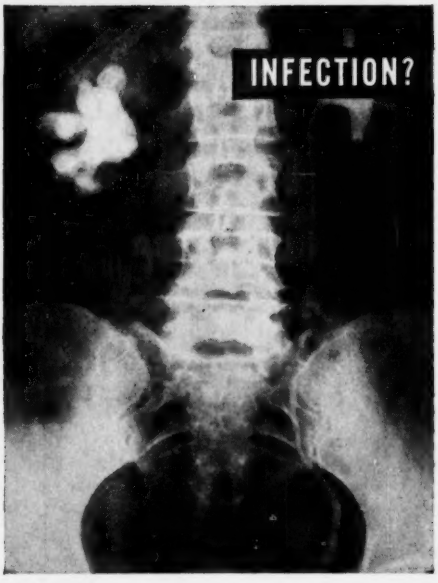

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